# ANNUAL REPORT
# OF
# PROGRAM ACTIVITIES
# CLINICAL CENTER
# FISCAL YEAR 1979

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United States. National Institutes of Health.
" Clinical Center

Report of Program Activities

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## OFFICE OF THE DIRECTOR

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# PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## OFFICE OF THE DIRECTOR

### General

The Clinical Center has continued to evolve both professionally and physically. Renovations have begun to integrate the Clinical Center with the Ambulatory Care Research Facility and to modernize the hospital. Professional services provided by the Clinical Center have been increased despite unchanging personnel ceilings. Intensive mutual reviews of Institute clinical research programs and Clinical Center support efforts have facilitated planning.

Clinical Center staff provided hospital services and, for the first time, direct physician care on a limited basis in its new medical intensive care unit. Department members conducted research in their own specialties to develop and improve current technology to meet the needs of the clinical programs and collaborated with Institute scientists. Opportunities for advanced training were provided to young physicians, medical students, nursing students, and members of the paramedical professions.

### Mission of the Clinical Center

(1) To ensure the highest possible level of medical care to each patient;
(2) To provide optimal resources and facilities for clinical research;
(3) To perform research on methods and systems involved in patient care and study;
(4) To disseminate information to professionals and to the public relevant to clinical investigation;
(5) To develop and maintain training programs in the techniques and ethics of biomedical research and clinical research;
(6) To interact with scientists and physicians, nationally and internationally, on mutual problems of clinical research, such as policy, education, ethics, and priorities.

### Ambulatory Care Research Facility and Clinical Center Modernization

ACRF construction continued on schedule and within budget. Last fall an 800-car subterranean parking garage was opened to NIH employees, and in July, the ACRF tower structure was "topped-off," the next milestone being building enclosure scheduled for this winter. A contract for ACRF interior design was awarded and a fine arts committee established.

The ACRF/Clinical Center Modernization Committee, representing the NIH community, continued to address programmatic, design and construction issues related to integrating the old and new facilities. Clinic space requirements, conference room assignments/administration, and policies governing the housing of large research animals were addressed. Proposals for a cyclotron and the establishment of an Intraoperative Radiotherapy program were also considered.

During the fiscal year a number of construction projects were completed or begun. The 10-D Intensive Care Unit was completed and placed into operation. Construction began on 6-D and 13-East to prepare the areas for NIMH and NCI patients respectively. Design and construction to reconstruct the 9-West patient care unit damaged by fire were also initiate. A new East entrance to the building was constructed and modification to the West entrance initiated. Finally, a new nurse call system was installed in all patient care units.

Significant design activity occurred throughout the year. Major projects included the B-2 Glassware and Media preparation area, ESCD lockers, and the 2-East NHLBI Surgery Patient Care Unit. Preliminary to future design, all patient care units were surveyed to identify user needs and an environmental study of NIMH units was initiated and completed.

## New Services

The Critical Care Medicine Department, which was established in 1977 to care for critically ill patients throughout the Clinical Center, took a major step forward in providing services when it opened the doors to its new medical intensive care unit April 30.

The five bed unit is highly automated to facilitate continuous monitoring and supervision of critically ill patients. Dr. Byron McLees has been named Chief of the Critical Care Medicine Department.

A gynecology consultation service was established this past year in collaboration with the National Naval Medical Center Department of Obstetrics-Gynecology.

An audiologist was hired this past year to provide audiological evaluation services to Institute investigators requiring such tests for their patients. To support this service the Clinical Center has allocated space for sophisticated equipment which it recently purchased.

A full-time hospital epidemiologist, David K. Henderson, M.D., was added to the Clinical Center Hospital Epidemiology Section on May 15, 1979. Dr. Henderson, who is certified in both Internal Medicine and Infectious Diseases, is now directing the Clinical Center Hospital Infection Prevention Program. The major aims of this program are to prevent the occurrence of nosocomial (hospital-acquired) infections and to prevent transmission of infection from patients to patient-care staff or to hospital visitors. Nosocomial infections will be monitored to find potentially improvable preventive measures.

## Office of the Assistant for Bioethics to the Director, CC

During the past fiscal year, this office carried forward a number of activities including:

(1) Assistance to the Director, CC, on ethical issues in protocol review with approximately 20 protocols.

The Director and Assistant co-authored an article on institutional review at the Clinical Center, published in Hastings Center Report, Feb., 1979.

(2) Consultation with patients, families, and physicians on ethics dilemmas in treatment and research.

(3) Planning a research project on informed consent and the family.

The Assistant for Bioethics to the Director, CC, with the assistance of Maxwell Boverman, M.D., a psychiatric consultant, has conducted 82 interviews with patients. Patients and their family members were interviewed about their perceptions of how they were treated in the informed consent process and whether their questions had been satisfactorily answered. None of these patients or family members complained of being treated in an unethical manner or showed dissatisfaction with the manner in which questions were answered. The two major problems identified by the investigators in informed consent have been "false reassurances" about risk information and "in-group" language (technical-medical) used by physicians. These interviews are part of a pilot study that will lead to a protocol that will investigate whether the systematic involvement of a family member (or friend) in the informed consent process will result in a better recall by the patient of risk information and more closeness between patient, staff, and family.

(4) Teaching a bioethics seminar (one per month) to the Administrative Council of the Department of Nursing, CC.

(5) Consultation with investigators on questions of ethics in the planning of research.

## Medical Board

The quality of patient care remained the focus of Medical Board discussions in 1978-1979. The topics considered ranged from efforts to comply with Joint Commission Accreditation of Hospitals (JCAH) standards for medical audit to planning for a minimal care facility and more efficient utilization of existing resources.

Patient care evaluation or medical audit is an accountability mechanism by which a hospital can demonstrate that the quality of care it provides for its patients is consistently optimal. The Medical Audit Committee of the Medical Board was extremely active in this endeavor under the leadership of Dr. Stephen Marx. Guidelines for committee operation were developed in addition to meeting the quantitative audit requirements of the JCAH. Qualitative analysis of the audits revealed several instances of inadequate or inappropriate care. Individual services or physicians were informed of the variations from established audit criteria and the required follow-up to be taken. Medical audit has served an important role in improving patient care through physician education. Audits completed in 1978 included:

Anesthesiology services
Use of Anticoagulants
Management of Cardiac Arrests
 (by the Arrest Team)
Diagnosis of Diabetes Mellitus
Use of Gentamycin
Diagnosis and Management of Hematuria
Diagnosis and Management of Hypercalcemia
Diagnosis and Management of Hypothyroidism

The availability and accuracy of medical records is also critical to the quality of patient care. The Medical Record Committee went to great lengths to get physicians to standardize the abbreviations used in the medical record and to eliminate the backlog of incomplete records. A special task force was established to examine the current state of the medical record and to recommend ways by which the record's bulk could be reduced and its portability and utility increased. Although it has not completed its work, the accomplishments of this ad hoc group are already beginning to appear.

Several major issues confronted the Board during the year. The Department of Health, Education, and Welfare proposed guidelines for research involving children. Wishing to remain at the forefront of research review, the Medical Board evaluated the guidelines and immediately implemented an adapted version.

Compensation of injured research subjects has been a topic of national interest among clinical investigators. Although the Department is still grappling with the issue of reimbursement/insurance, regulations have been issued requiring investigators to advise prospective patients of the current state of affairs with regard to compensation or lack thereof. The Medical Board established standard language for inclusion on all general admission consent forms (and for protocol consent documents at the investigators/Institute's discretion).

In an effort to increase utilization of existing resources, the Clinical Center proposed the establishment of a minimal care facility. The plan specifically recommended the conversion of Building 20 (apartment house) to motel-type rooms. This topic was the subject of several discussions prompted by the original proposal, scientific directors' rejection of the proposal, and an NINCDS proposal to utilize the facilities of a local nursing home. The Board members went on record to favor the establishment of a minimal care facility and to resurface the Building 20 proposal.

Credentials review expanded to include the redelineation of clinical privileges. In addition physicians were required to certify their health status for the first time. The Credentials Committee reviewed seventy new applications for membership on the guest or consultant medical staffs. Only one was not subsequently approved by the full Board.

## Safety

Clinical Center Multi-Disciplinary Committee activity continued to develop and expand. Two major emergency incidents occurred this year - a stowstorm in February and a fire in April - which challenged the effectiveness of our disaster pre-planning. In both instances, personnel reacted in a prompt, highly satisfactory manner to protect patients, visitors, and staff from harm. A thorough critique of both incidents was completed and corrective measures started.

New program directions included: establishing a training-orientation program for professionals from the Bureau of Medical Devices, Food and Drug Administration; promoting and implementing an autoclave quality control program; assisting Division of Engineering Services in conducting tests of emergency power generators; consummating a medical device recall/reporting system; assisting in ACRF and Clinical Center construction plan review.

Program expansion continued in: disaster planning; safety rules on use of flammable/toxic gases; environmental surveys; corridor use and clearance; safety program publicity through use of bulletin boards, seminars, and *Closeup*; and a refined accident/incident reporting system.

## Office of the Associate Director

### 1. The Clinical Associate Program

Recruitment for the Clinical Associate Program continues to be a matter of high priority because of a continuing decline in the pool of available trainees. Each year there are approximately 249 physicians (200 Clinical, 49 Research) in the Associate Program. The associates spend two to three years at the Clinical Center and are Board qualified in most subspecialties at the termination of their training. Training in internal medicine is not approved for Boards in except in the National Heart, Lung and Blood Institute and this further limits the numbers of applicants.

The Clinical Center has initiated an aggressive advertising campaign aimed at medical students and recent graduates. This involved distribution of brochures and flyers to students, their advisors, and other faculty. This year 1,482 applications were requested compared to 850 in 1978. Three hundred and two completed applications were received, representing a 30%

increase over the preceding year. In the actual matching process, 83 candidates were accepted compared with 75 for the preceding year. The following chart describes the number of associates matched in 1979 for the years 1980 through 1982.

| | TOTAL | 1979 | 1980 | 1981 | 1982 |
|---|---|---|---|---|---|
| CLINICAL ASSOCIATES | 62 | 7* | 42 | 12 | 1 |
| DENTAL CLIN. ASSOC. | 1 | 1 | | | |
| RESEARCH ASSOCIATES | 19 | | 9 | 10 | |
| STAFF ASSOCIATES | 0 | | | | |
| PRAT | 1 | | 1 | | |
| TOTAL | 83 | 8 | 52 | 22 | 1 |

*Early Selections

As of July 1, 1979, the majority of available positions for 1980 had been filled, with no difficulty anticipated in filling in the few remaining positions. Applicants continue to apply one year in advance of proposed training in contrast to previous years when most positions were filled two years in advance. The consensus is that the quality of the candidates for Associateships is equal to or better than that experienced previously. Selectees for 1980-1981 trained at 53 teaching hospitals throughout the United States.

The 1979 matching program was reviewed by the Education Committee. An effort will be made during this coming year to familiarize institute personnel with the matching process well in advance of the date on which applicants are selected. The brochures and catalogs for the 1980-1981 recruiting have been revised and redesigned.

### 2. The Clinical Electives Program

The following eight-week courses were offered to third and fourth year medical students: Medical Genetics, Hematology-Oncology, Anesthesiology, Computers, Infectious Disease, Immunology, Endocrinology and Metabolism, Psychopharmacology, Nuclear Medicine and Surgical-Oncology. During this year a new elective in Child Psychopharmacology was offered by Dr. Judith Rapoport, NIMH, and the Surgical-Oncology elective, NCI, was expanded to include students during the summer months. The numbers of applicants to these programs continues to increase: 115 students from 60 medical schools participated in the 1978-1979 Elective Program, as compared to 120 during 1977-1978.

Brochures describing the electives were distributed to second and third year medical students and their advisors. Dr. Shapiro and Dr. Richard Knazek, NCI presented a seminar on NIH and Biomedical Research Training to the Organization of Student Representatives, The Association of American Medical Colleges, at their October, 1978, meeting.

## 3. The Participation of Minority Physicians in NIH Training Programs

Those racial and ethnic groups traditionally under-represented in medicine are also underrepresented in biomedical research. As of July 1, 1979 10% of the entering class of clinical associates were women as compared to 6.5% the preceding year. Five percent of the associate group were Black and there was one clinical associate of Hispanic origin, these proportions have not changed recently.

Minority representation in the Associate Programs at NIH was the subject of a workshop sponsored by the Clinical Center in March of 1979. Representatives from the "minority" and "majority" medical schools, the AAMC and NIH, met to discuss steps which could be taken to increase minority representation at the Clinical Center. A number of concrete proposals were developed by this group, several of which subsequently received the approval of the Director, NIH.

Dr. Shapiro addressed the Annual Meeting of the Student National Medical Association in Los Angeles, July, 1979, and subsequently met with Black medical students from Duke University Medical School, the University of North Carolina to inform them about student electives and graduate research training opportunities at the Clinical Center. It was hoped that each of these groups would communicate to their colleagues the fact that the electives program would be an excellent way for students to gain insight into research careers.

An initiative involves 1) assisting expansion of the MBS and MARC programs by stimulating the submission of requests for MBS and MARC Awards from minority schools, and 2) allowing NIH to compete for those NHSC Scholarship recipients who choose to repay their service obligation doing research.

## 4. Clinical Center Departments

A. The Medical Information System (MIS): The MIS system has been fully implemented in the hospital for the past year. As it now functions, it is probably the most comprehensive system based in any hospital in the United States. During this time there has been substantial revision of preexisting protocols, addition of new protocols to the system, and extensive redevelopment of other software. This office has assisted OCAMS in the management of the implementation process and has facilitated interdepartmental relationships within the Clinical Center and between the Clinical Center and the Technicon Corporation. A major addition this year was the laboratory results reporting link which became operational on July 1, 1979. Prior to the activation of this component, there were several preliminary, yet major, additions which involved a new specimen collection system, and the

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development of a link between the Technicon computer and the laboratory's Honeywell computer. Each step in the implementation required training in one or another department. The training program for entering Clinical Associates was redesigned this year with favorable results. This year the MIS system will be expanded to the Outpatient Department. Hospital-wide use of the MIS system has stimulated a reevaluation of the current methods of record keeping on hospital units and in the Outpatient Department. A department-by-department evaluation of the MIS system as it currently functions in the Clinical Center has been initiated. For this purpose a series of survey questionnaires based on the original MIS impact statements developed by OCAMS staff. This initial evaluation will be completed by December of 1979 and precedes a larger hospital-wide evaluation which will extend over the next two years.

B. Medical Staff Affairs: The Office of Medical Staff Affairs (OMSA) has as its main function the coordination of the hospital's Quality Assurance Program (QAP). In this role it remained the clearinghouse for all intramural clinical research projects and provided the required staffing for Medical Board committees.

Approximately two hundred (200) new clinical projects were approved over the last year bringing the total number of active studies to over 625. The office also monitored the periodic review of all existing projects. This included the processing of over 400 annual reviews and 150-200 three-year reviews. The issuance of new regulations on research involving children was the main source of investigator inquiries requiring OMSA responses.

Credentials review, another cornerstone of a QAP, entered a new dimension with the first re-delineation of clinical privileges. Almost 350 physicians and dentists were required to have their clinical privileges reviewed and their health status certified. Seventy-three new applications for clinical privileges were processed by the office and forwarded to the Credentials Committee. Forty-nine guest medical staff and twenty-three clinical care consultant applications were approved. In addition, one physician assistant was granted staff affiliate status.

Staff assistance was also provided to the Medical Audit Committee of the Clinical Center. This endeavor included the completion of the eight required audits for 1978 and starting the eight 1979 audits.

C. The Normal Volunteer Program: The annual report from the Normal Volunteer Program is included on page __. The Program reports through the Office of the Associate Director to the Director of the Clinical Center. A standard contract for cooperating institutions and organizations has been developed. The number of colleges sending volunteers to NIH has been increased with the addition of Ohio State and the reactivation of the Alderson-Broaddus College contract. The Lions Club of the Washington area has agreed to supply outpatient volunteers to the Normal Volunteer Program. As of September 1979, the NIH has contracts with 22 organizations which supplied a total of 433 inpatients and 3,337 outpatient volunteers this year. In addition, there were 2,800 off-site visits made to homes and schools, in all, representing a 31% increase in visits by outpatient volunteers during 1979.

D. Surgical Administrative Committee: The Associate Director serves as the chairman of the Surgical Administrative Committee. This committee is a forum for Institute and Clinical Center departments utilizing the hospital's surgical facilities and has been enhanced by the presence of the newly appointed operating room manager, Mr. Michael Jauriguizar. During its monthly meetings this committee has considered matters such as staffing, safety, back-up electrical services, and surgical suites planned for the Ambulatory Care Research Facility.

E. Continuing Medical Education (CME): NIH staff have shown increasing interest in AMA category 1 CME credit because of pressure from state and professional organizations, particularly for relicensure. Under the sponsorship of the Education Committee an increasing number of lecture series and rounds at the Clinical Center have been reviewed and approved. In addition, certain NIH off-campus educational programs have also received approval. There are 30 courses or rounds now certified, many of these are listed weekly in the NIH Calendar and identified as approved for category 1 credit. On July 25, 1979, the Clinical Center was accredited for four years by the Liaison Committee on Continuing Medical Education, thereby facilitating the granting of CME credit to NIH educational events.

The Office of the Associate Director coordinates the FAES Medicine 610 review course which runs from September through May and has approximately 75 to 100 participants including medical students, clinical associates, and physicians from the community.

## 5. Research and Teaching

In collaboration with Dr. George Martin, NIDR, and Dr. James Hansen, NICHHD, research has been conducted in clinical and biochemical abnormalities in osteogenesis imperfecta. This study has been incorporated into the weekly genetics outpatient clinic where patients with osteogenesis imperfecta and other brittle bone diseases are seen and utilized for teaching purposes. An investigation of the possible defects in collagen systhesis in these patients is being conducted in collaboration with Dr. David Rowe, Department of Pediatrics, University of Connecticut, Farmington. Also, during the year, teaching rounds were presented to the Department of Endocrinology, George Washington University, at Pediatric Rounds, NICHHD, and at the post-clinic Endocrine Conference, Clinical Center.

## Research Accomplishments

This year, the Blood Bank Department, in collaboration with NIAID researchers expanded their studies on non-A, non-B hepatitis. Two of the most significant developments were: 1) the finding that a very high proportion (approximately 50%) of patients with acute non-A, non-B hepatitis developed chronic hepatitis and 2) the finding that chimpanzees developing non-A, non-B following human blood inoculation stratified into two distinct categories. Electronmicroscopy revealed that some chimpanzees developed a distinct intranuclear structural change in their liver cells while others developed distinct cytoplasmic tubular structures. Serial biopsies were obtained from each animal and there was never any overlap between the two groups, i.e., each animal had either nuclear

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or cytoplasmic change, but not both. These structural changes were specifi for non-A, non-B hepatitis and suggest that there may be at least two age responsible for this disease. In the absence of a serologic test for non-A non-B hepatitis, these structural changes represent the first specific mark for non-A, non-B agents.

Clinical Center investigators, together with scientists from the NCI and th NHLBI, demonstrated the effectiveness of young erythrocytes in transfusion support of patients with thalassemia major. Despite improved iron chelator usage, transfusion-induced hemochromatosis remains a significant limiting factor in the survival of patients with thalassemia major. Selective tra fusion with young ethrocytes (neocytes), which have a longer lifespan than routine donor cells, has decreased the frequency of transfusion and will th reduce iron deposition. The CC investigators modified existing techniques using available continuous flow blood cell component systems to prepare units of young erythrocytes from normal donors for transfusion support. The use of neocytes with their prolonged survival in combination with continuous parenteral chelator therapy may offer a means to achieve iron balance in patients at risk for transfusional hemochromatosis.

In the Rehabilitation Department, investigators have successfully used biofeedback techniques in patients with Raynaud's phenomenon to normalize thei responses to decreases in environmental temperatures. Of 20 patients with either primary or secondary Raynaud's phenomenon exposed to $3.3^{\circ}$ C, 19 succ successfully used two biofeedback techniques to abort a classic attack of this condition. Researchers in the Rehabilitation Department are in the process of evaluating the long-term results of biofeedback in these patie

Members of the Nuclear Medicine Department, in collaboration with NHLBI's Pulmonary Branch and DCRT's Laboratory of Applied Studies, developed noninvasive procedures to study regional lung function in patients with pulmonary fibrosis, emphysema and other lung diseases. The use of nuclear imaging equipment makes possible the rapid measurement of radioisotope distribution in pulmonary alveolar and capillary beds. This allows evalua of ventillation-perfusion matching which is the main determinant of respiratory gas exchange. Results are analyzed by a computer and are displayed either as images (regional perfusion, lung volume, ventillation) or as movies of dynamic regional function. Because these procedures can b used to evaluate regional pulmonary function, they are expected to provide a sensitive means of following disease progression and response to therapy

Investigators in the Diagnostic Radiology Department, in collaboration with the Pharmacy Department, developed an intravenous contrast material (EOE 13) containing ethiodized oil in an emulsion form to selectively opacify the liver and spleen for computed tomographic examination, which facilitates earlier detection of liver metastases. Following preclinical toxicity studies on rats and monkeys, an Investigational New Drug permit w obtained from the Food and Drug Administration, and phase I clinical studi were started in January, 1979. To date, researchers in the Diagnostic Radiology Department have examined 10 patients; visualization of liver les in some of the patients was significantly improved. Investigators intend to continue clinical experiments with slightly larger doses of contrast material.

Members of the Clinical Pathology Department investigated the application of the radioimmunoassays for isoenzymes MM and BB of creatine kinase to patients with schizophrenia and neuromuscular disorders. They also completed the first phase of a study of the use of the CK-BB assay in prostatic cancer. Preliminary results indicated that CK-BB is a new tumor marker for prostatic carcinoma and may have value in the early diagnosis of the disease. Studies continue on the use and improvement of the serum CK-BB radioimmunoassay in myocardial infarction, cardiac surgery and in prostatic and other cancers. The use of CK-BB as a tumor marker for prostatic and other cancers appears particularly promising.

The nursing research program defined the mechanisms used to review nursing research proposals identical to that of the Institute review process. Through this modality, in collaboration with biomedical scientists in the Heart, Lung, and Blood Institute, nursing staff documented nursing occupational exposure from patients receiving diagnostic radionuclides. It was found that ambulatory patients receiving diagnostic radionuclides expose nursing personnel to low levels of ionizing radiation, but the amount of exposure was less than the maximum permissible dose for pregnant or potentially pregnant females. Further studies of radiation exposure to nursing personnel and other biomedical personnel from patients receiving diagnostic radionuclides are needed in hospital areas where contact hours with patients are greater than 3-6 hours, e.g. intensive care units or post-surgical units.

## EEO

On March 16, 1978 the Clinical Center hosted an all day workshop designed to develop strategies to increase the participation of minority physicians in biomedical research training programs. The primary objective of the conference was to identify mechanisms that might be utilized to increase the number of minority physicians in the Associate Training Programs at NIH. Participants in this workshop included representatives from Howard, Meharry and Morehouse Colleges of Medicine, Albert Einstein, the King Drew Postgraduate Medical School, and the University of Texas at San Antonio. Also present were representatives from the Association of American Medical Colleges, the NIH Education Committee and the Office of the Director, NIH. Several Clinical Associates and Extramural Associates also joined in discussions. Several recommendations were developed at this meeting which, given the proper management support, should have significant impact on the problem of recruiting minority physicians at the NIH.

For the first time, Affirmative Action was included in the NIH Director's Forward Plan Review Sessions. The EEO Coordinator was asked to discuss the Clinical Center's Affirmative Action initiates along with the senior administrative staff at the Clinical Center Forward Plan presentations on November 30, 1978. Clinical Center employees elected the following representatives and alternates to the EEO Advisory Committee: Ms. Susan Gerhold and Ms. Marguerite Smallwood, Office of the Director; Ms. Rose Lawrence and Mr. Neil French, Diagnostic Radiology and Nuclear Medicine Departments; Mr. Frank Greenwell and Mr. George Gaskins, Fabric Care Department; Ms. Geri Mann and Ms. Mary Aber, Social Work, Rehabilitation and Spiritual Ministry Departments; Ms. Yasmin McMahon and Ms. Purnell Cofield, Medical Records Department; Mr. Harvey Pippins and Ms. Betty Malone, Critical Care Department; Ms. Novella Oglesby and Mr. Cero Hayes, Pharmacy Department; Ms. Ernestine Wood and Ms. Beth Green, Clinical Pathology and Blood Bank Departments; Ms. Minnie Todd and Mr. Coleman Chandler, Property Management and Transportation Section, Mr. Thomas Bonnar and Ms. Cathy Hawkins, Outpatient Department; Ms. Rita Aukward, Mr. Joseph Hambrick, Ms. Alfrieda Nagata and Ms. Patricia Herlihy, Nursing Department; Mr. William Hubbard, Ms. Mary Wellons, Ms. Vergie Carter and Mr. Symes Haynes, Environmental Sanitation Control Department.

EEO Awards were presented to Mr. Charles Brooks, Surgical Services Department; Mr. Neil French, Diagnostic Radiology Department; Ms. Jean Green, Environmental Sanitation Control Department; and Ms. Catherine Quigley, Nuclear Medicine Department.

## Office of Clinical and Management Systems

### I. Missions and Goals:

The mission of the Office of Clinical and Management Systems is to assist the staff of the Clinical Center by providing services of systems analysis, computer systems evaluation, and management engineering.

The goals are four fold:

a) Coordinate the planning, development, implementation, and operation of all computer and automated systems within the Clinical Center;

b) Provide working liaison between the Clinical Center, the Division of Computer Research and Technology, and the various Institutes to assure optimal and integrated clinical management and information systems;

c) Assist Clinical Center Management in application of techniques of operational planning; facility development; resource allocation; and program evaluation and review; and,

d) Initiate and conduct research and education programs in clinical and management systems.

### II. Department Activities:

A. Medical Information Systems: Continuing implementation of the Computerized Medical Information System (MIS) occupied the largest portion of the office's activities during this year.

The link between MIS and the Clinical Pathology Computer System was completed both for ordering and result reporting. This is a major milestone not only in the Clinical Center's information processing, but also in the history of such systems in the Clinical Center's information processing, but also in the history of such systems in the entire field. Daily handling of over 14,000 result entries in a way that makes this critical medical information instantly available to the physicians has involved hardware and software development. The Laboratory Order/Result Link probably is the most significant feature of MIS for the physician user. Based on the previous experiences in training physicians for MIS, a revision to the self-instructional modules was developed and implemented so that over 100 new physicians were able to have their training and work with MIS in their patient care activities immediately upon their arrival here. The success of the self-instructional modules in physician training was such that similar packages were designed for nursing and pharmacy. A discharge care plan was implemented to consolidate the information required by nurses for continuity of patient care. This feature also aids in meeting one of the major requirements in nursing of the Joint Commission on Accreditation of Hospitals. User input and system monitoring generated over 1,000 change requests during this year, many of which were related to the addition and modification of clinical protocol order sets. The standardization of protocol order sets and the documentation of their contents has been a major advance in medical management for the hospital. The OCAMS staff also has interacted with the data processing and the medical and administrative staffs of several large hospitals and university medical centers around the country who are in the process of assessing their needs for MIS type systems in their institutions. The experience with MIS at the Clinical Center has provided a rich source of unique information for these colleagues in the field. With the system largely installed as of this time, several evaluative steps have been taken. Early in the year a study was made of the comparison between processing of medication and intravenous therapy orders with a total manual system versus MIS. The overwhelming conclusion based on nursing and pharmacy workload measurements was that MIS provided a superior method of handling these orders from the point of view of their accurate, complete, and timely transmission to the pharmacy and to the man-hour requirements of the professional staff in assembling and working with these orders. At the behest of the Medical Board, two formal system-wide evaluation processes were begun. First of these was called the "mini evaluation" and involved questionnaire data gathering on a department-on-department basis in the Clinical Center for a qualitative evaluation on a feature by feature basis of MIS effectiveness in that department's work environment. The second, more extensive evaluation involves the use of departmental set-aside funds for hiring contractors to thoroughly evaluate all aspects of MIS as it relates to the future use of the system in the Clinical Center and its effectiveness in this setting. The proposals for set-aside funding were accepted at the DHEW level and RFP development is in process as the year ends.

B. Clincal Information Utility: The clinical information utility which stores medical information at DCRT and retrieves it on request for medical researchers in the various Institutes began enlarging its role in serving the needs of the staff throughout the campus. In addition to providing individual researchers with numerous retrievals on laboratory, medication, diagnosis, and biographic data in various combinations, the CIU also became a valuable tool to the Quality Assurance Committee of the Medical Board in streamlining the process of performing medical audits. Both in selection of sample records to be reviewed as well as an analysis of the content of these records, the CIU data base has become an integral part of the medical audit process and makes possible the completion of these audits in a more timely fashion with a much more thorough review than is possible under purely manual methods.

C. Laboratory Computer System: The Chief, OCAMS, continues to serve as the Chief, Laboratory Computer Service, Clinical Pathology Department during this year. All of the programming for the Honeywell side of the MIS-Clinical Pathology Link was done by staff of the Laboratory Computer Service under the supervision of the Chief, OCAMS. In addition, design was completed on interface hardware for the new Colter CBC and platelet analyzer so that these results can be fed electronically into the Honeywell System without need for manual transcription in the near future. The close oversight of Honeywell programming efforts and MIS. design and implementation efforts on the link enabled the two systems to be interfaced and maintained with a high degree of quality and data integrity.

D. Workload reporting and budgeting system for Clinical Center Departments: During the year, the RMS (Resource Monitoring System) continued to serve as the Clinical Center's portion of the agency-wide manpower management program. Steps were begun to update the nursing portion of the RMS to reflect more accurately the utilization of manpower in nursing service for the coming years. OCAMS staff joined with the financial management office to develop a new set of budget reporting documents. These documents were developed to assist department heads monitor their budget activities in a timely and accurate fashion. With this year's emphasis on cost containment, the executive office and departments were better able to monitor their use of funds.

E. Nursing Classification and Staff Report: By incorporating data provided by the nursing service, OCAMS staff developed an operational system whereby graphic analysis of the changing mixes of patients and the changing requirements for nursing manpower on a unit-by-unit basis could be analyzed. This was a major addition to the management tools available to the CC OD and the Nursing Department.

F. Medical Record Improvement Projects: Staff was involved at several levels in maintenance and improvement of the quality of medical records. First, a staff member chaired the Medical Record Forms and Systems Sub-committee of the Executive Medical Record Committee of the Medical Board. This sub-committee was instrumental in screening new forms proposed for inclusion in the medical record as well as in defining a large number of forms which are no longer to be used or kept in stock. The "Medical Record Improvement Project" Committee addressed issues of chart bulk as well as usefulness of information as it is presented in the medical record. OCAMS staff provides the support to this project group in questionnaire design and evaluation, coordination with DCRT, and systems analysis to enable recommendations of the committee to be integrated with ongoing operations in information handing throughout the hospital.

G. Outpatient Department Study: OCAMS staff provided professional guidance and staff support to a study of the operations of the outpatient clinics. This study was undertaken to provide a smooth transition of MIS functions into the clinic, upgrade the general services provided for physicians in the outpatient setting, and develop operational models for conducting outpatient services in the ACRF. Data gathering and graphic representation of clinic operations has been completed. Plans were devised for the implementation of diagnostic radiology ordering on outpatients as the next step in the integration of MIS into the OPD.

H. CLINFO Test Site: OCAMS provided space and professional support for a trial of CLINFO at the NIH. CLINFO is a prototype data management and analysis system using computers for storage, retrieval, and analysis of data pertaining to medical research. Though originally developed for general clinical research centers, the DRR-funded CLINFO system may have applicability for the intramural programs as well. This test arrangement was established to enable NIH staff to try CLINFO and examine possibilities for its use in their own research.

I. Material Management: The staff continued to assist the ACRF Project Officer in developing specifications for the material handling systems and in conducting the recruitment effort for a chief of materials management. This has enabled the office to remain current with the developments in the material handling systems so that when they become integrated into the hospital setting they can be managed appropriately.

J. Professional Activities: OCAMS provided a large segment of the teaching for the NIH computers in a clinical medicine program, an annual program coordinated by DCRT. A paper was prepared and presented at the working conference on hospital information systems in Capetown, South Africa. Staff members also made a presentation to the annual meeting of the American Society of Hospital Social Workers. A staff member, as Conferences' Chairman of the Health Services Division, American Institute of Industrial Engineers, coordinated a program on microprocessor applications in health care. A staff member has served on the USPHS Engineer Career Development Committee. The Chief, OCAMS, completed his term as President of the Medical Information Systems Association (MISA). OCAMS staff participated actively in a working conference on the development of Ancillary Services Review for the PSRO Program and also for the development of a shared Management Engineering Program for a consortium of several community hospitals in Baltimore. The staff is also represented on the Executive Committee of the Maryland Hospital Education Institute in the capacity of Second Vice-Chairman of the Board of Trustees and in participation in the American College of Surgeons Patient Safety Project for the development of an information system for patient safety. The staff participated as faculty for the Medical Record School of the USPHS in Baltimore by developing and presenting a series of lectures in "Computers in Medicine."

K. Staffing: OCAMS staff was augmented by the addition of a STRIDE student in the field of Computer Science. Though the office was successful in recruiting a candidate for the open Management Analysis position, a hospital-wide staffing reduction eliminated this slot, so the full-time staff remained at three.

## III. Future Objectives:

A. The MIS installation in Outpatient Services is a primary objective for the coming year. Only when this phase of the installation is complete can MIS be evaluated as a "total" hospital information system.

B. Because the current contract for MIS services expires at the end of FY 80, extensive efforts will be made to review the MIS specifications and contractual arrangements to assure continuity of service into the future.

C. As the Honeywell laboratory computer system reaches its fifth year of operation, the specification and acquisition of a replacement system for laboratory computing will be undertaken. A five year system life was anticipated for the Honeywell configuration when it was purchased in 1974.

D. Staff support will be sustained for the Medical Record

Improvement Project. These will be directed toward the final design and logistics involved in a greatly improved presentation of Clinical Pathology data for the physician in patient care and research. The other thrust in this project for which OCAMS will have major responsibility will be in attempting to change the form in which major sections of the medical record are kept from paper to electronic storage medium.

E. With the re-organization of the Financial Management Office, CC, and the further revision of budget reporting and control systems, OCAMS has as an objective the complete integration of the Resource Monitoring System for workload and manpower management reporting into the budget process and the transfer of operational responsibility for this to the FMO.

F. With the set-aside project for evaluation of the Medical Information System scheduled for contract award in FY 80, the OCAMS staff will be involved extensively in the evaluation process, including providing the Project Officer, for the contract. In addition, the department-by-department "mini-evaluation" will complete the data-gathering phase and result in a report to the Medical Board on this portion of MIS evaluation.

G. It is expected that the test site evaluation of CLINFO will be completed and a decision reached as to whether further NIH resources need to be allocated to make CLINFO available to the clinical research staff on an ongoing basis.

H. Ongoing support will be given to all CC departments as they seek to develop their expertise in computerization. The Nutrition Department will be assisted in its evaluation of an advanced computer system for management of its functions.

I. A staff member will chair a national conference on the application of industrial/management engineering to the improvement of health care systems.

## Office of Clinical Reports and Inquiries

Clinical Center information, publications, press, and public affairs activities are centered in the Office of Clinical Reports and Inquiries. The office is responsible for advising the Director and Executive Staff on ways to enhance the Clinical Center's public and professional image as a preeminent clinical research facility, and on the effective interpretation and reporting of research findings produced within the Center. These findings are of interest and concern to many audiences, including Congress, the Department and other Government agencies, scientists, physicians, voluntary health agencies, and the general public.

The Office initiates many programs and responds to Congressional and Departmental, NIH, and internal and public requests. It keeps all Clinical Center personnel informed of hospital activities, provides all hospital departments with communications assistance, and supports the functions of the CC's hospital service departments to ensure the delivery of the highest quality of patient care.

## Staff Communications

Physician Recruitment: A year ago OCR&I together with the Associate Director's Office launched an aggressive national recruiting campaign to attract top candidates to the NIH medical elective and associate training programs.

The plan called for continuous exposure throughout the year using journal advertisements, direct mailings of brochures and flyers, and selective mailings of catalogs and other materials to key individuals and institutions that could disseminate this information or make it available to students.

In addition to helping institutes write and place advertisements in journals about their own "fellowship" programs, we developed and placed generic ads announcing opportunities for all NIH training programs.

To simplify access to specific information about Institute programs in this year's catalog, a matrix was developed that enables the reader to find out at a glance whether a topic is being studied and which Institute(s) is involved in the research.

OCR&I has updated all recruiting publications and will again arrange for their distribution.

Some Institutes seem to have benefited more than others from this program. Nevertheless, the results are encouraging. Recruiting is a long-term endeavor wherein results are usually cumulative. We have every reason to expect even better results next year.

The OCR&I helped to develop an Associate Training program exhibit that will be displayed at meetings around the country. The exhibit was completed in the spring and shown at the Student National Medical Association annual meeting in Los Angeles. A member of the Information Office staff accompanied a clinical associate to man the exhibit.

Department Pamphlets and Displays: Promoting employee communications remains an important goal for OCR&I since success in this area contributes to the sense of unity and community essential to the smooth operation of the hospital. Last year the information office worked to unify all CC publications and establish a Clinical Center identity.

A number of new publications now in circulation conform to this style. The office presently is working with the Medical Arts Department to develop a Clinical Center logo that can be used on publications and on other materials originating from the Clinical Center.

Publications were prepared or revised for a number of departments including, the Medical Record Department, Clinical Pathology Department, Nursing, Patient Representative, Office of the Director, the Blood Bank, Employee Health Service, Normal Volunteers, Outpatient Department, Office of Clinical and Management Systems.

Staff coordinated the travel and display of exhibits for the Department of Anesthesiology and the associate director's office.

Closeup: The Employee newsletter Closeup appeared monthly and continued to provide Clinical Center employees with timely news about the place they work and the people they work with. Employees were kept up to date on construction and renovation activities, including the opening of the ACRF parking garage, the ceremonial topping off celebration marking the completion of the ACRF superstructure, and the relocation of departments and clinics following renovations.
OCR&I staff worked closely with the CC Safety Committee to prepare a 4-part series on safety which was reprinted and distributed desk to desk. Closeup was also on hand to cover the drama of the recent fire emergency and February's snow emergency and the courageous and selfless responses of CC employees and area residents.

The quest to improve our newsletter is ongoing. An editorial board was established this year to serve as a forum for new ideas. To facilitate newsgathering and obtain better representation from the various departments, OCR&I sent out a call to the departments for correspondents to alert Closeup to newsworthy items. The Closeup editor attended a two-day course on newsletter writing and design.

Director's Newsletter: OCR&I continued to assist the CC Director in preparing Director's Update, a newsletter for communicating clinical and administrative information to hospital physicians.

### Patient Communication Program

OCR&I is continuing to develop a comprehensive information program for Clinical Center patients.

A series of leaflets on tests and diagnostic procedures will soon be available to patients. Nearly 50 of these documents which were prepared by the Nursing Department and edited by this office will include a questionnaire and, when appropriate, a map showing the location of the testing site.

Patients also will benefit from a series of maps and a directory which will be included in the patient handbook soon.

The unique nature of the CC and the role that its patients play in research makes the upcoming publication on informed consent particularly important both for the patients and the clinical care staff. The manuscript was written by Drs. Philippe Cardon and John Fletcher, edited by OCR&I, and reviewed by the medical board and several CC departments before being submitted to the printer. It is hoped that this publication will help incoming patients understand their rights and responsibilities and clarify for them their role in the research environment of the Clinical Center.

Related to this publication is a videotape on informed consent that is being produced by OCR&I for airing on the patient channel of the CC's new closed circuit television system. The script for the tape was recently completed and a production schedule is being planned for the fall.

Closed Circuit Television System: OCR&I continued on its course to activate the patient channel of the closed circuit television system. This channel, which will be devoted primarily to health related programs presented in layman terms, represents an alternative to commercial televison.

Patients will have an opportunity to learn about issues that affect their health and what they can do to improve their well being. Other programs will be aimed at orienting the patient to the Clinical Center and to the activities that they can participate in; explaining their role as participants in research protocols; and helping them identify places of interest in Washington in the event that they or their families have an opportunity to sight see.

A television advisory board was established this past year to assist in the implementation of the patient education television system and to serve as a focus for policy matters relating to the system. Members include Ruth Carlsen and Jean Harris, Department of Nursing, Dr. Jay Shapiro, Associate Director, CC, Dr. John Fletcher, Assistant for Bioethics, CC, Steven Galen, Administrative Officer, CC, and Doreen Mead and Lanny Newman (Chairman), OCR&I.

The channel will begin operating August 31. A comprehensive plan was developed for patient television programming. Previewing and purchasing of appropriate shows is underway. OCR&I staff has met with a number of centers operating closed circuit television systems. Most notable was a meeting with Elizabeth Norris, vice president for education, Greater Cleveland Hospital Association, and her staff in Cleveland. GCHA operates an 18-hospital television network and provides the programming for an experimental satellite system that presently is beaming two hours of patient education programs to participating hospitals daily. Ms. Norris and her team were able to offer many sound suggestions and practical advice to help us prepare for our opening date.

As part of a reorganization within the Clinical Center, the television engineering section became an operating component of the OCR&I. The chief of the section, Mr. Will Whitehouse, will supervise the technical operations of the closed circuit system.

The system to feed program material to the patient antenna distribution system is ready for use pending minor adjustments and optimization by the contractor Antronriex Antenna Systems, Inc. We will be able to accomplish limited production assembly and titling with our monochrome system but any outside color videotapes will come through in living color.

Presently this section gives particular support to the following branches: Cardiology Branch, NHLBI, Diagnostic Radiology, Ultrasound, Echocardiography, Nuclear Medicine, the Laboratory of Parasitic Diseases, NIAID, and Diagnostic Methodology, NIDR.

## Cardiology Branch, NHLBI

Support consists of videotaping of the ventricular cineangiograms, coronary arteriograms, and the newly instituted procedure for coronary dilitation. Extensive use is made of the television facilities to record, playback, and analyze the video image for data pertinent to the patient's diagnosis and care (e.g. ejection fraction, and regurgitant index).

## Diagnostic Radiology

The staff is on call for videotaping and playback for numerous procedures carried out in the Diagnostic Radiology Branch (e.g. Barium Swallows, Voiding Cystourethrograms, Arteriograms, etc.).

These are either played back for immediate review, held for playback at conference time or used in the stop motion made for direct photography as a permanent record in the patient's chart.

## Ultrasound

A real time ultrasound scanner, the Learle B scan format, the NBS Computer enhanced image or the ADS linear array scan are sent to T.V. Engineering for recording playback and still frame photodocumentation.

A new utilization of the real-time scanner is its application to pharyngeal structure analysis during speech. This will lead to several papers describing the new technique and its application in the study of abnormal phonation.

## Echocardiography

The section recently cabled up to the Echo Lab to record playback and analyze the echocardiograms. We are using the crispener to enhance detail in the images. Extensive use of our facilities by the echo lab has generated several titled composite videotapes depicting various valvular diseases.

## Nuclear Medicine

A unit is being purchased by Nuclear Medicine to convert their computer images of normalized ventricular cycles from the computer scan to the television format. This will enable us to store the image for later replay to the conference room during rounds. As a result of our being a central viewing facility, all these images relating to a single patient (e.g. the cineangios, echocardiograms, and the Nuclear Medicine ventriculograms) can be shown to the surgeon during open heart surgery for a refresh of fluid dynamics.

## Laboratory of Parasitic Diseases

An extensive television system using low light level cameras is employed by the laboratory to visualize and record faint microscopic images under monochromatic light.

This is utilized to study cell proliferation, growth patterns and the effect of various pharmacologic agents on the cultures in vivo.

## Diagnostic Methodology

This branch is actively engaged in the computer analysis of video images derived from dental radiographs. Contrast enhancement, differentiation of edges and crispening techniques are applied to the computer images. Our function will be storage of dynamic transforms for later replay and to develop the intercommunication capabilities between various branches who are engaged in computer analysis of video images.

The OCR&I provides patient recruiting services to Clinical Center physicians needing patients for particular research studies. In addition to revising the Current Clinical Studies and Patient Admission Procedures and distributing it to physicians around the country, the office prepared announcements of new protocols and sent them to area physicians to notify them of the latest NIH intramural clinical programs to which they may nominate patients.

To determine whether CC clinicians could use assistance in recruiting patients for their studies, the OCR&I prepared and distributed a questionnaire to Institute physicians. Early returns indicate that most physicians are satisfied with their recruiting programs but some would welcome OCR&I help.

## Clinical Reports and Scientific Publications:

This office coordinated seven Combined Clinical Staff Conferences this year and edited the proceedings of six of them for publication in the Annals of Internal Medicine. Approximately 35,000 notices were mailed to referring area physicians on the availability of these papers in reprint form and over 8,000 reprints went to requestors.

These conferences and the proceedings are an important means of sharing with scientists and physicians all over the world the most recent research findings, and techniques developed by NIH investigators.

The office edited 124 professional papers prepared by CC staff for publication in medical and scientific journals and provided editorial services during manuscript preparation.

Seven nursing conferences were presented this year by members of the Clinical Center Nursing Department. This office helped prepare the programs and publicity (table tents, flyers, invitations, posters) for the conferences. In addition OCR&I edited the conferences for publication as monographs for distribution to nurses across the country.

## Public Communications Program

One of the missions of the Clinical Center is to disseminate information to professionals and to the public relevant to clinical investigation. The Center's unique status brings together leading researchers whose work at the frontiers of science produces many important advances in understanding the nature of diseases and in caring for patients.

## Medicine for the Layman

To disseminate some of this information to the public, the Clinical Center two years ago initiated a series of health seminars called "Medicine for the Layman." Leading NIH scientists presented timely and informative talks that covered normal body function and what can sometimes go wrong.

The series proved to be highly popular among many Greater Washington residents. Word of its success traveled surprisingly far with organizations from around the country requesting advice on setting up their own programs.

This success prompted the OCR&I to develop a series of pamphlets and videotapes based on the lectures for national distribution.

Several Institutes have requested separate printings of some of the publications for their own use. Arrangements are underway with the National Audiovisual Center to market and distribute the videotapes as they become available. Several organizations have asked for our videotapes, even though we have yet to begin our promotional campaign.

## Public Inquiries

The OCR&I receives numerous calls and letters asking about admission policies and/or information relating to diseases or health care. Approximately 360 patient referrals to the Clinical Center from private physicians were processed through this office.

The office also answered approximately 200 Congressional and general inquiries by letter and telephone.

## Press

Press and media activity was high for the Medicine for the Layman series. During the month of September, 1979, Channel 5's Panorama featured Dr. Lipsett and two lecturers for the 1979 series (Dr. Gillin and Dr. Andres). Four other lecturers will appear on the show in the next two months to promote the series. Channel 9's P.M. Magazine and many radio stations will air our Public Service announcements throughout the fall. All newspapers in the area carried announcements about this year's series. Special mention was made of the series in the _Washingtonian_ and _Washington Calendar Magazine_.

The office assisted the United States Information Agency in a filming assignment for use in a telethon to be aired in Chile. The Rehabilitation Department was the government setting used to film crippled children undergoing therapy.

OCR&I placed a story in the _Montgomery Journal_ on a student from Johns Hopkins who is working in Dr. Harvey Gralnick's hematology laboratory (Clinical Pathology). The work of Donald Morisato was of such high quality that he was invited to present his paper at the American Society of Hematology.

The OCR&I coordinated a platelet donation drive in Annandale, Virginia, for the Tri Delta alumni association and helped produce a 30-second T.V. and radio spot featuring Jerry Smith of the Washington Redskins.

The April 21 Clinical Center fire prompted innumerable calls from the radio, T.V., and print media. OCR&I staff fielded press calls throughout the emergency and for a number of days following.

Various Institutes called on the OCR&I to assist them in press events of national importance. Dr. Gary Peck, Dermatology Branch, NCI, was interviewed frequently at the Clinical Center because of his successful treatment of patients with acne. Other news features filmed at the Clinical Center with various Institutes' participation included Dr. Donald Calne (NINCDS) with a patient with Parkinson's disease, Dr. Joan Bull (NCI) with a patient with cancer being treated by hyperthermia, and Dr. Neal Young (NHLBI) who discussed treatment for thalassemia.

## Special Events

The Special Events Staff planned, coordinated and directed specific programs for 43,860 visitors to the NIH in FY 1979. Included were 261 visitors from 37 foreign countries and 1,339 domestic visitors. The Section consulted, planned and provided staff assistance for 220 scientific and administrative meetings attended by 42,521 visitors in the Jack Masur Auditorium.

During the FY 1979, the Special Events Section engaged in the following:

Scheduled 182 appointments with NIH researchers

Arranged 116 film showings for 778 visitors

Conducted 138 tours for 858 visitors

Collected, assembled and distributed 5,862 publications to visitors

Collected, assembled and distributed 36,130 publications for lecture series "Medicine for the Layman"

Answered 1,562 public inquiries by letter and telephone

Maintained the NIH Speakers Bureau and filled 20 requests

Administered roster of individuals and called upon them to assist in interpreting for 9 foreign visitors and foreign born patients

Maintained a current and comprehensive invitation list for all NIH Lectures, dedications and ceremonies

As executive secretary for NIH Lecture Committee, was responsible for administrative arrangements for 2 NIH Lectures, 2 G. Burroughs Mider Lectures and the R.E. Dyer Lecture

# NIH LECTURE SERIES
## Fiscal 1979

The Special Events Section is responsible for administrative arrangements for the NIH Lectures.

R.E. Dyer Lecture:
October 18, 1978 Attendance: 500
Frank H. Ruddle, Ph.D.
Professor of Biology and Human Genetics
Yale University
New Haven, Connecticut
Title: "Gene Transfer in Mammalian Cells"

NIH Lecture:
December 6, 1978 Attendance: 450
Beatrice Mintz, Ph.D.
Senior Member
Institute for Cancer Research
Fox Chase
Philadelphia, Pennsylvania
Title: "Turning Cancer Cells Into Mice"

R.E. Dyer Lecture:
March 14, 1979 Attendance: 400
Elvin A. Kabat, Ph.D.
Professor of Microbiology, Human Genetics and Development
Columbia University
College of Physicians and Surgeons
New York, New York
Title: "Structural and Genetic Approaches to the Study of Antibody Complementarity"

NIH Lecture:
May 2, 1979 Attendance: 400
Robert T. Schimke, M.D.
Professor of Biology
Stanford University
Standford, California
Title: "Gene Amplification and Methotrexat Resistance in Cultured Mammalian Cells"

NIH Lecture:
June 13, 1979 Attendance: 450
Professor Albert Elsen
Department of Art
Stanford University
Stanford, California
Title: "In Rodin's Studio: The Sculptor and Photographers"

## SPECIAL EVENTS SECTION ACTIVITIES

## Comparison-Fiscal Years 1971-1979

| | VISITORS | | | MEETINGS | | TOURS | | MOVIE SHOWINGS | | APPOINTMENTS WITH STAFF | REQ. FOR SPEAKER | PUBS. DISTRIBUTED | INQUIRIES | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| YEAR | For. | Dom. | Total | No. | Attendance | No. | Attendance | No. | Attendance | | | | PUB. | CONG. |
| 1971 | 629 | 2,533 | 3,162 | 215 | 48,156 | 241 | 1,210 | 388 | 2,605 | 583 | 44 | 23,663 | 1,792 | 2 |
| 1972 | 900 | 2,846 | 3,746 | 231 | 40,785 | 211 | 1,172 | 330 | 2,760 | 610 | 23 | 32,521 | 1,875 | 4 |
| 1973 | 1,010 | 2,489 | 3,499 | 241 | 48,648 | 179 | 852 | 343 | 2,315 | 651 | 56 | 31,237 | 1,660 | 6 |
| 1974 | 529 | 2,232 | 2,761 | 194 | 47,804 | 175 | 932 | 228 | 1,340 | 804 | 37 | 21,983 | 1,620 | 1 |
| 1975 | 416 | 23,184 | 23,600 | 258 | 51,368 | 167 | 1,078 | 229 | 1,654 | 498 | 31 | 75,777 | 1,482 | 1 |
| 1976 | 510 | 22,837 | 23,347 | 68 | 19,974 | 157 | 602 | 189 | 1,799 | 504 | 9 | 69,750 | 1,433 | 0 |
| 1977 | 2,505 | 1,574 | 2,079 | 298 | 55,742 | 238 | 1,192 | 275 | 1,282 | 461 | 47 | 11,374 | 1,346 | 25 |
| 1978 | 297 | 2,374 | 2,671 | 264 | 62,360 | 240 | 1,531 | 246 | 1,352 | 363 | 28 | 9,738 | 1,501 | 9 |
| 1979 | 261 | 1,078 | 1,339 | 220 | 42,521 | 138 | 858 | 116 | 778 | 182 | 20 | 5,862 | 1,556 | 6 |

## DISTRIBUTION OF VISITORS BY CONTINENTS

### Fiscal Years 1974 - 1979

| CONTINENT | FY - 1974 | FY - 1975 | FY - 1976 | FY - 1977 | FY - 1978 | FY - 1979 |
|---|---|---|---|---|---|---|
| AFRICA | 9 | 7 | 80 | 34 | 11 | 3 |
| ASIA | 266 | 143 | 121 | 219 | 146 | 149 |
| AUSTRALIA | 12 | 4 | 2 | 7 | 5 | 0 |
| EUROPE | 142 | 129 | 166 | 212 | 113 | 98 |
| NORTH AMERICA | 2,312 | 1,764 | 42,941 | 1,587 | 2,380 | 1,084 |
| SOUTH AMERICA | 20 | 25 | 11 | 20 | 16 | 5 |
| TOTALS | 2,761 | 2,072 | 43,321 | 2,079 | 2,671 | 1,339 |

# VISITORS DURING FISCAL YEAR 1979 - BY DISCIPLINE

## A. Domestic - 1,078

| | | | |
|---|---|---|---|
| Medical | 231 | Medical Educators | 3 |
| Paramedical | 202 | Employees | 41 |
| Administrative | 46 | Technology | 1 |
| Hosp. Admin. | 24 | Clergy | 1 |
| Teachers | 4 | Congressional | 23 |
| Grad. School | 140 | Journalist | 50 |
| College | 243 | Interpreter | 2 |
| High School | 47 | Laymen | 20 |

## B. Foreign - 261

| | | | |
|---|---|---|---|
| Lab. Science | 88 | Laymen | 5 |
| Medical | 108 | College | 2 |
| Paramedical | 13 | Engineers | 4 |
| Administrative | 29 | Statesmen | 2 |
| Hosp. Admin. | 1 | Minister of Health | 2 |
| Teachers | 2 | Grad. School | 5 |

Foreign Visitors by Country of Origin - Fiscal Year 1979

| | |
|---|---|
| Africa | 1 |
| Austria | 1 |
| Belgium | 2 |
| Brazil | 3 |
| Canada | 6 |
| China | 37 |
| Cyprus | 1 |
| Czechoslovakia | 2 |
| Denmark | 1 |
| Ecuador | 1 |
| Egypt | 1 |
| England | 9 |
| Finland | 1 |
| France | 5 |
| Germany | 4 |
| West Germany | 1 |
| Greece | 2 |
| India | 9 |
| Indonesia | 2 |
| Iran | 1 |
| Israel | 3 |
| Italy | 36 |
| Holland | 5 |
| Japan | 78 |
| Kuwait | 1 |
| Luxemburg | 1 |
| Norway | 6 |
| Pakistan | 1 |
| Philippines | 4 |
| Poland | 13 |
| South Africa | 1 |
| South America | 1 |
| Syria | 1 |
| Sweden | 4 |
| Switzerland | 3 |
| USSR | 12 |
| Yugoslavia | 1 |

## SPECIAL EVENTS SECTION

| MONTH | VISITORS | | | MEETINGS | | TOURS | | NIH MOVIE SHOWINGS | | APPT. WITH STAFF | REQUESTS FOR SPEAKERS | REQUESTS FOR INTERPT. | PUBS. DISTRIB-UTED | PUBLIC INQUIRIES |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | For. | Dom. | Total | No. | Attend-ance | No. | Attend-ance | No. | Attend-ance | | | | | |
| OCT. | 43 | 51 | 94 | 19 | 5,610 | 10 | 91 | 7 | 43 | 12 | 1 | 1 | 445 | 303 |
| NOV. | 3 | 158 | 161 | 20 | 4,715 | 6 | 12 | 8 | 114 | 9 | 4 | - | 515 | 125 |
| DEC. | 1 | 11 | 12 | 12 | 3,330 | 3 | 12 | 1 | 1 | 2 | 6 | - | 89 | 75 |
| JAN. | 5 | 68 | 73 | 11 | 2,370 | 9 | 68 | 6 | 9 | 7 | 2 | - | 245 | 110 |
| FEB. | 10 | 87 | 97 | 25 | 4,130 | 9 | 89 | 6 | 86 | 11 | 2 | - | 887 | 125 |
| MARCH | 44 | 153 | 197 | 33 | 4,696 | 7 | 68 | 5 | 120 | 14 | 2 | - | 785 | 140 |
| APRIL | 9 | 111 | 120 | 20 | 2,502 | 14 | 105 | 15 | 115 | 10 | 1 | - | 657 | 125 |
| MAY | 63 | 124 | 187 | 26 | 4,683 | 22 | 135 | 11 | 64 | 26 | 1 | - | 704 | 120 |
| JUNE | 21 | 41 | 62 | 16 | 3,715 | 14 | 51 | 10 | 45 | 17 | 1 | - | 287 | 145 |
| JULY | 15 | 130 | 145 | 8 | 2,055 | 14 | 127 | 13 | 97 | 32 | - | - | 752 | 94 |
| AUG. | 35 | 75 | 110 | 7 | 1,444 | 19 | 25 | 23 | 58 | 31 | - | 1 | 247 | 104 |
| SEPT. | 12 | 69 | 81 | 23 | 4,860 | 11 | 75 | 11 | 26 | 11 | - | 1 | 249 | 90 |
| | | | | | | | | | | | | | | |
| TOTAL | 261 | 1078 | 1339 | 220 | 42,521 | 138 | 858 | 116 | 778 | 182 | 20 | 3 | 5,862 | 1,556 |

## Professional Activities

Dr. Lipsett was elected to the office of President of the Endocrine Society at the Annual Meeting held in Anaheim, California, June 13-15. He served as Secretary General, International Society of Endocrinology. He was elected to membership on the National Board of Trustees of the American Physicians Fellowship and accepted the appointment of Clinical Professor, Department of Medicine, Uniformed Services University of the Health Sciences.

Dr. Lipsett continued to serve as Associate Editor of *Cancer Research* Editorial Board and on the Board of Editors for *Monographs on Endocrinolog*

Dr. Lipsett participated as Discussion Leader on Cancer and Hormones at the NCI-INSERM Conference on Endocrinology held at Seillac, France, October 23-26, and attended the Fifth International Congress on Hormonal Steroids, New Dehli, India, October 30-November 4, where he presented a paper on "The Role of Testosterone in Regulation of LH." Other conference participation included a Conference on Clinical Research at the University of Chicago Center for Policy Study, the Consensus meeting on Steroid Receptors in Breast Cancer held at NIH (as rapporteur), and the Twelfth Annual Meeting of the Society for the Study of Reproduction, Laval University, Canada.

Seminars and lectures given by Dr. Lipsett included: "Current Concepts in Ovarian Physiology and Function" at the Cook County Hospital, Chicago; "Steroid Production, Interconversion and Metabolism," "Effects of Drugs on Hormones," and "Male Hypogonadism," as Visiting Professor of Endocrinol at UCLA; "Drugs and Hormones" at the 31st Annual Midwest Cancer Conference Topeka, Kansas; "Testicular Function in Health and Diseases" at the University of Michigan Reproductive Endocrinology Program; "Problems of Carcinogenesis" at the Endocrine Society Annual Meeting; and "Improved Patient Care through Research and Education" at Upjohn Co. meeting of medical science liaison representatives.

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## NORMAL VOLUNTEER PROGRAM

### I. General Statement:

Fiscal Year 1979 was a successful year for the Normal Volunteer Program All needs of the research investigators were met for the in-patient, out-patient and off-site studies. College students continued to be the mainstay of the long-term in-patient program. They supported our biomedical research goals and honored their commitment to the research studies. They performed with exceptional honesty and integrity on lengthy and demanding studies and adjusted well to the restricted and difficult conditions of living in a hospital environment. Sponsoring colleges and universities actively supported our program. Local community and religious resources continued to fill our increasing need for short-term in-patient volunteers and for out-patient volunteer quickly and effectively.

Students continued to take advantage of career assignment opportunities All were placed in career assignments corresponding to their academic interests and career goals. This aspect of the Normal Volunteer Program is a major factor in developing and maintaining interest in ou program by students and college and university officials as well as providing a purposeful activity for each volunteer during his/her stay in the Clinical Center. The success of this program is shown by the enthusiasm of all concerned, the colleges, the students, and the preceptors.

Stress was placed on improving the quality of the Normal Volunteer Program. Continued effort was made to improve the effectiveness of informed consent procedures. Volunteers were encouraged to accept more responsibility themselves for understanding protocols before agreeing to participate. They were urged to question and discuss with the investigator any area, such as the purpose, demands, length of stay etc., which was not clear. Medical, nursing and administrative staff made greater effort to understand the individual volunteer's problems when faced with the rigid restrictions and demands of biomedical research studies and the daily difficulties and frustrations of healthy young people living in a hospital environment. This alleviated some of the behavior problems encountered in the past. The support of Dr. John Fletcher, Assistant to the Director for Bioethics, has been of great help to both staff and volunteers in developing understanding of the responsibilities of everyone involved in biomedical research. Forms were devised for volunteers' use in evaluating each protocol in which they participated. Some questions asked: Was the protocol followed? Were there changes or additions? How were you treated by staf etc. These evaluations are being carefully reviewed.

Concerted effort was made to up-date and expand informational material concerning the Normal Volunteer Program. The "Handbook of the Normal Volunteer Program at the Clinical Center", for the use of medical and nursing staff, has been revised. An audio-visual program is being developed for use in recruitment and interview meetings. A new poster has been designed for recruitment purposes. A former volunteer's personal version of life as a volunteer is being approved for printing and should be helpful in familiarizing volunteers and interested applicants with the day-to-day aspects of the program. Also, a new certificate of appreciation has been designed to be given to each volunteer on completion of his stay at the Clinical Center.

The Medical Board approved an increase, effective January 1, 1979, in the per diem for in-patient volunteers and in the hourly rate for OPD and off-site volunteers. This was the first increase since May 1975 and more accurately covers rising expenses due to inflation. This increase has enabled some students to participate in the program who could not afford to otherwise.

Prospects for the coming year are excellent. The contracting sponsors are enthusiastically and effectively supporting the program and an increasing number of people are interested in participating. Continued stress on the bioethics of biomedical research and improvement in the informed consent process have improved the quality of the program. Increasing rapport between medical and nursing staff and volunteers and continuing worthwhile career assignment have eased the adjustments of volunteers to the biomedical research studies and the difficulties of living in a hospital environment.

## II. IN-PATIENT PROGRAM

The overall in-patient program has remained relatively consistent with past years. The same eight Institutes continue to use in-patient volunteers, but there has been an increasing need for volunteers by NINCDS. Statistically, the number of in-patient volunteers remain about the same. However, this actually represents a slight increase (approximately 10%) in the number admitted to the Clinical Center this year since volunteers at the NIAMDD Research Unit of the Phoenix Indian Medical Center are no longer included in our program. The daily census usually ranged from 50-65 volunteers representing about 15% of the total Clinical Center in-patient census. The total number of days and the average length of stay for each volunteer was less than last year due to the increase in short-term studies conducted by NIMH and NINCDS. Note the following table.

| | NO. OF VOLS. | TOTAL NO. DAYS | AVERAGE DAYS PER VOL. |
|---|---|---|---|
| FY 1978 | 434 | 21,519 | 49.58 |
| FY 1979 | 433 | 16,701 | 38.57 |
| Decrease | 1 | 4,818 | 11.01 |

The cost of the in-patient program decreased slightly from last year (about 12%) in spite of the increase in per diem effective in January 1979 and increased travel costs. This again is the result of the many short-term studies conducted using volunteers from local community resources.

| FISCAL YEAR | EXPENDITURES |
|---|---|
| 1978 | $ 323,586.00 |
| 1979 | - 283,773.00 |
| Decrease | $ 39,813.00 |

## III. OUT-PATIENT AND OFF-SITE PROGRAM

This portion of the Normal Volunteer Program fluctuates from year to year depending on the research projects being conducted, i.e. duration of project, number of visits required, and length of each visit. There was a dramatic increase in both programs this year; a 31.2% increase in OPD visits over last year, and over six times more off-site visits. This increase is due primarily to the infant and child development studies being conducted by NIMH and NICHD. All requests for volunteers were filled, but difficulty was met in finding healthy men and women, ages 55 to 75 years, willing or able to participate. The cost of the OPD program increased by 53% and the off-site program by almost 700% from last year. This increase is due to the extensive increase in visits and total hours and by the increased hourly reimbursement for volunteers effective January 1979. Please note the following tables:

PER CLINIC VISITS

| | VISITS | TOTAL HOURS | EXPENDITURES |
|---|---|---|---|
| FY 1979 | 3307 | 11,020 | $ 82,937.00 |
| FY 1978 | 2520 | 7,695 | - 53,002.00 |
| Increase | 787 | 3,325 | $ 29,935.00 |

OFF-SITE VISITS

| | VISITS | TOTAL HOURS | EXPENDITURES |
|---|---|---|---|
| FY 1979 | 2838 | 5,527 | $ 24,509.00 |
| FY 1978 | 435 | 793 | - 3,328.00 |
| Increase | 2403 | 4,734 | $ 21,181.00 |

## IV. VOLUNTEER RESOURCES

Our contracting resources have continued to meet the needs of the program. Two new contracts have been written this year and one has been reactivated. This gives us 13 active college and university sponsors for long term in-patient volunteers and 9 local community resources for short-term OPD and off-site studies. A new contract with the Ohio State University Research Foundation in Columbus, Ohio, and the renewed interest at Alderson Broaddus College in West Virginia improves our in-patient, long-term volunteer selection. A new contract with the Lions International - District 22C in Maryland adds to our short-term in-patient and OPD studies. Two other colleges in Minnesota and Iowa continue to show interest and discussions are being conducted with them. However, at this time there is a question whether more contracts are needed, as we have more applicants than openings.

With the appointment in June 1978 of an assistant to the Chief, Normal Volunteer Program, closer contact has been maintained with contracting resource personnel. This has been extremely important due to new staffing at the various schools who are unfamiliar with our program. All sponsoring colleges were visited this year for group discussions and interviews. In additions, more administrators and professors from the various colleges visited the Clinical Center to familiarize themselves with the program and to see first hand the educational opportunities for their students.

The question of liability should harm or injury occur to a volunteer as a result of a research study has been of increasing concern to sponsors. Our rigid screening of protocols for approval, effective informed consent procedures, and our past record in the use of normal volunteers has alleviated some of the apprehension.

One other area of concern we are facing is the energy problem. Whether the increased cost of gasoline and long lines at the pumps will affect our OPD studies is uncertain. Undoubtedly, travel conditions will affect our travel to the various sponsors making trips more difficult and time consuming.

## V. SPECIAL INCIDENTS

No medical misadventures were reported this fiscal year, but there are some areas that should be noted. Volunteers continue to find long metabolic and restrictive diet studies very difficult. Tensions have been eased by the increased awareness of the medical and nursing staff to the individual needs of the volunteers. Living in a hospital, particularly on a psychiatric unit, is difficult for healthy young people. Close support by medical, nursing, and administrative staff plus more available recreational activities help this situation. The YMCA has donated 5 passes for Clinical Center volunteers and these have been in continual use and sincerely appreciated by the volunteers.

Another area of concern is the use of volunteers on studies up to the time of discharge. One or two have been discharged slightly anemic o with a slightly elevated blood pressure. It is strongly urged that studies be completed in advance of discharge, if possible, to give the volunteer time to readjust - and to reflect on his experience at the Clinical Center in a healthy, positive frame of mind.

It also should be noted that one volunteer, while on pass, was struck by a car when riding his bicycle. He was given all appropriate medical and supportive care and then discharged at his request. We have not been notified of any further problems.

## VI. CAREER DEVELOPMENT

The career development aspect of the program continues as a strong motivating factor for colleges and universities and their students to participate. All students were placed on career assignments according to their academic fields and career goals. As in past years most are majoring in pre-medicine, the biological-chemical sciences, psychology, or affiliated fields. This year we did have some students interested in computer programming, journalism, and art therapy and these too were placed in appropriate positions. The students and their respectiv colleges are most enthusiastic and appreciative of this learning experience. The preceptors who guide and work with these young people are equally enthusiastic, finding them bright, hard-working, inquisitiv and dependable and a valuable asset to their research team.

## VII. AGE RANGE

The age of in-patient volunteers during this fiscal period ranged from six to 72 years, with college age students, 19 to 22 years, constitutin the largest groups. Over 90% of the volunteers remaining in the Clinic Center for 3 to 4 months or more were college age students. However, they comprised only about 53% of the total in-patient group due to the increased number of short term studies.

## VIII. SEX RATIO

The percentage of male and female volunteers is dictated primarily by the nature of the medical research studies. In past years we have frequently had to replace requests for men and women. This year we have had more than enough men applying and all investigators' needs were met for both men and women. Of the 433 in-patient volunteers, 232 were men (53.6%) and 201 were women (46.4%).

## CHART # 1

## TOTAL ESTIMATED* EXPENDITURES BY AGENCY FOR FISCAL YEAR 1979

| AGENCY | AMOUNT |
|---|---|
| Alderson-Broaddus College | $ 920.00 |
| California State University, Chico | 47,609.00 |
| Church of the Brethren General Board | 37,665.00 |
| Church of Jesus Christ of L.D.S., (Mormon) Frederick Ward | 423.00 |
| Church of Jesus Christ of L.D.S., (Mormon) Gaithersburg Ward | 4,454.50 |
| Church of Jesus Christ of L.D.S., (Mormon) Kensington Ward | 1,585.00 |
| Church of Jesus Christ of L.D.S., (Mormon) Rock Creek Ward | 4,817.25 |
| Davidson College | 7,550.00 |
| Gustavus Adolphus College | 20,972.00 |
| Indiana State University, Terre Haute | 4,729.00 |
| Kalamazoo College | 19,333.00 |
| Keuka College | 12,254.00 |
| Mental Health Association of Montgomery County | 98,347.25 |
| Montgomery College | 8,753.00 |
| Pennsylvania State University | 15,107.00 |
| University of California, Davis | 63,750.00 |
| University of California, Santa Cruz | 25,908.00 |
| Warner Memorial Presbyterian Church | 2,115.00 |
| Wittenberg University | 14,541.00 |
|  | $390.833.00 |

*July, August, September 1979 estimated

CHART # 2

TOTAL ESTIMATED* EXPENDITURES BY INSTITUTE FOR FISCAL YEAR 1979

| INSTITUTE | AMOUNT |
|---|---|
| NCI | $ 25,006.25 |
| NIAID | 63,188.00 |
| NIAMDD | 34,239.00 |
| NHLBI | 58,828.25 |
| NICHD | 55,633.50 |
| NIMH | 136,855.50 |
| NINCDS | 6,321.50 |
| NEI | 10,281.00 |
| NIDR | 480.00 |
|  | $390,833.00 |

*July, August, September 1979 estimated

## CHART # 3
## NUMBER OF VOLUNTEERS, TOTAL DAYS & EXPENDITURES (In-Patient)*

October 1, 1978 to September 30, 1979

### BY INSTITUTE

| INSTITUTE | VOLUNTEERS | TOTAL DAYS | AMOUNT |
|---|---|---|---|
| NIAMDD | 30 | 2178 | $ 34,239.00 |
| NCI | 12 | 758 | 13,278.00 |
| NICHD | 48 | 2852 | 48,525.00 |
| NIDR | -- | -- | ---- |
| NEI | 8 | 578 | 10,027.00 |
| NHLBI | 68 | 3304 | 58,292.00 |
| NIAID | 67 | 3696 | 63,188.00 |
| NIMH | 137 | 3202 | 53,125.00 |
| NINCDS | 63 | 133 | 3,099.00 |
| | 433 | 16,701 | $283,773.00 |

### BY AGENCY

| AGENCY | VOLUNTEERS | TOTAL DAYS | AMOUNT |
|---|---|---|---|
| Alderson-Broaddus College | 2 | 50 | $ 920.00 |
| California State University, Chico | 25 | 2740 | 47,609.00 |
| Church of the Brethren General Board | 53 | 2369 | 37,665.00 |
| Church of L.D.S., Frederick | 5 | 22 | 346.00 |
| Church of L.D.S., Kensington | 26 | 59 | 1,371.00 |
| Church of L.D.S., Rock Creek | 3 | 6 | 141.00 |
| Davidson College | 11 | 528 | 7,550.00 |
| Gustavus Adolphus College | 21 | 1346 | 20,972.00 |
| Indiana State University, Terre Haute | 6 | 348 | 4,729.00 |
| Kalamazoo College | 17 | 1229 | 19,333.00 |
| Keuka College | 22 | 727 | 12,254.00 |
| Mental Health Assoc., Montgomery Co. | 132 | 681 | 11,528.00 |
| Montgomery College | 1 | 3 | 49.00 |
| Pennsylvania State University | 18 | 978 | 15,107.00 |
| University of California, Davis | 52 | 3340 | 63,750.00 |
| University of California, Santa Cruz | 21 | 1291 | 25,908.00 |
| Wittenberg University | 18 | 974 | 14,541.00 |
| | 433 | 16,701 | $283,773.00 |

*July, August, & September 1979 estimated

CHART # 4

## ESTIMATED* OUT-PATIENT REPORT FOR PERIOD OCTOBER 1, 1978 - SEPTEMBER 30, 197

### BY AGENCY

| AGENCY | TOTAL VISITS | TOTAL HOURS | AMOUNT |
|---|---|---|---|
| Church of L.D.S., Gaithersburg | 277 | 309 | $ 3,811.50 |
| Church of L.D.S., Kensington | 18 | 20 | 214.00 |
| Church of L.D.S., Rock Creek | 351 | 442 | 4,521.25 |
| Mental Health Assoc., of Mont. Co. | 2382 | 9546 | 68,610.25 |
| Montgomery College | 270 | 682 | 5,595.50 |
| Warner Memorial Presby. Church | 9 | 21 | 184.50 |
|  | 3307 | 11020 | $82,937.00 |

### BY INSTITUTE

| INSTITUTE | TOTAL VISITS | TOTAL HOURS | AMOUNT |
|---|---|---|---|
| NCI | 963 | 976 | $11,460.00 |
| NICHD | 504 | 560 | 6,746.50 |
| NIDR | 21 | 65 | 480.00 |
| NEI | 15 | 43 | 301.25 |
| NHLBI | 10 | 80 | 536.25 |
| NIMH | 1662 | 8900 | 60,224.50 |
| NINCDS | 132 | 396 | 3,188.50 |
|  | 3307 | 11020 | $82,937.00 |

*July, August, September 1979 estimated

## CHART # 5

## ESTIMATED* OFF-SITE REPORT FOR PERIOD OCTOBER 1, 1978 to SEPTEMBER 30, 1979

### BY AGENCY

| AGENCY | TOTAL VISITS | TOTAL HOURS | AMOUNT |
|---|---|---|---|
| Church of L.D.S., Frederick | 7 | 21 | $ 77.00 |
| Church of L.D.S., Gaithersburg | 86 | 128 | 643.00 |
| Church of L.D.S., Rock Creek | 31 | 31 | 155.00 |
| Mental Health Assoc., Montgomery Co. | 1928 | 4337 | 18,595.00 |
| Montgomery College | 592 | 597 | 3,108.50 |
| Warner Memorial Presbyterian Church | 194 | 413 | 1,930.50 |
|  | 2838 | 5527 | $24,509.00 |

### BY INSTITUTE

| INSTITUTE | TOTAL VISITS | TOTAL HOURS | AMOUNT |
|---|---|---|---|
| NCI | 51 | 51 | $ 255.00 |
| NICHD | 58 | 74 | 362.00 |
| NIMH | 2729 | 5402 | 23,892.00 |
|  | 2828 | 5527 | $24,509.00 |

*July, August, September 1979 estimated

## PATIENT ACTIVITIES DEPARTMENT

### I. DEPARTMENT MISSIONS AND GOALS

This year, the primary mission of the Patient Activities Department was to provide a diversified, patient-centered program of therapeutic recreation activities and library services to all patients of the Clinical Center, both in-and outpatients. Thes programs were designed to meet the physical and psychological needs, interests, and capabilities of Clinical Center patients and to be consistent with medical research objectives. Department goals included:

The education or re-education of the patient in the construct use of his leisure, during hospitalization and after discharg

The elimination of boredom, and as a result, to help alleviat stress and anxiety

The introduction of a variety of new recreation and cultural opportunities to the patient

The support needed to help the patient regain or reinforce hi self esteem

The provision of emotional and psychological support to the patient and his family

The adaptation of leisure activities for the patient, based o his physical and emotional needs, and on his individual research protocol

The continuation, as much as possible, of the patient's normal leisure activities during periods of hospitalization.

All programs were organized, executed, and evaluated under the guidance of a professional staff of therapeutic recreation specialists and assistants.

### II. DEPARTMENT ACTIVITIES

### A. Therapeutic Recreation Section

1. Adult Recreation Referral Program
Based upon a written referral from the attending physic this program featured creative arts and crafts, and spo

activities. This year, of the 3690 patients referred to this particular program, 2337 (approximately 63%) participated. For a more detailed statistical breakdown, see Attachment #1, Item #1.

As part of this program, 378 different patients were worked with on their unit on a one-to-one basis. A special bedside program for 7 East patients involved 189 patients in a program of social and creative craft activities.

2. Adult Social Program
This program featured seasonal events, dances, musical programs, trips, feature films, and many other appropriate social activities. This year, there were 324 activities planned, with 10,609 patient/family participants.

   As part of this program, recreation activities were offered for patients and family members at the United Inn (SACP). This year there were 183 activities planned, with 2448 patient/family participants.

3. Children's Play Programs (All Institutes)
A creative and diversified play program was offered to all child patients, siblings, and child visitors. Activities were held predominantly in the 14th Floor Playroom. This year, 905 different child patients and child visitors were involved in the program. For a more detailed statistical breakdown, see Attachment #1, Item #2.

   As part of this program, 99 different child patients required bedside visitations.

4. Institute Programs: Therapeutic recreation activities geared to meet specific patient/Institute needs.

   a. National Institute of Mental Health (2 West, 3 East & West, 4 East & West)
   This year, 667 different patients were involved in this program. For a more detailed statistical breakdown, see Attachment #1, Item #3.

   b. National Cancer Institute
      1) Pediatric Oncology
      Unit 2 East/2B: This year, 668 different patients were involved in this particular program.
      OPD-West Clinic: This year, 1135 different patients and 197 siblings were active in this program.

2) Special Unit Programs (10 East, 12 East & West, 13 East)
This year, 2448 different patients were involve in these programs. For a more detailed statistical breakdown, see Attachment #1, Item #4.

c. NINCDS: This year, 906 different patients were involved in this program.

## B. Patient's Library Section

### 1. Books

| | |
|---|---|
| Inventory | 6950 |
| New Acquisitions | 209 |
| Lost in Circulation | 50 |
| Discarded | 144 |
| Circulation (patients & personnel) | 9685 |
| Via Library | 7021 |
| Via Bookcarts | 2630 |
| Inter-library loan | 34 |

### 2. Patients Contacted

| | |
|---|---|
| Visiting Library | 5934 |
| Visited on Unit (bookcart) | 8212 |

### 3. Magazines

| | |
|---|---|
| Subscriptions | |
| Monthly | 71 |
| Semi-monthly | 46 |
| Bi-monthly | 2 |
| Bi-weekly | 3 |
| Weekly | 15 |
| Quarterly | 1 |
| Circulation | 8476 |
| Average Monthly | 706 |

### 4. Newspapers

| | |
|---|---|
| Subscriptions | |
| Washington Post | 28 |
| Wall Street Journal | 1 |
| Christain Science Monitor | 1 |
| Circulation (Washington Post) | 10192 |

5. Reading Utilization - See Attachment #2

## III. MAJOR PROGRESS IN SERVICES/TRAINING/DEVELOPMENT

### A. Department Status

This past year, the Patient Activity Section was organizationally removed from the defunct Patient Services Department and granted Department status. This move has fostered closer communication with Clinical Center administration and other Department heads, and has strengthened our role as an accepted member of the Clinical Center's allied health services.

### B. Patient Library

1. Hyperactive Study: Mrs. Swim, Library Supervisor, continued to be an integral part of the 2 West Mental Health interdisciplinary team, giving the children on that unit extra reading time. She was required to evaluate the specific patient behavior in relation to the type or quality of drug intake. There was a total of 20 children involved in this program for an average of thirteen weeks' stay. Mrs. Swim worked with three children a week, two hours per week with each child.

2. Library Use: The Patients' Library experienced a definite decline in the number of patients visiting the library. We attribute this to the fact that there was a reduction of the number of patients in the hospital. Also, the patients who were in the hospital seemed to be quite ill, and therefore unable to leave the unit. Most of these patients looked forward to having the bookcart visit them and did enjoy magazines and lighter, picture type books to peruse.

### C. Pediatric Oncology

1. In-Patient Service (Units 2 East/B)
   A reorganization of the staffing for this program enabled a full-time therapeutic recreation specialist to be solely assigned to the Laminar Air Flow Unit (2B). A newly allocated 35 hour therapeutic recreation specialist position, as well as a 20 hour student position were then assigned the responsibility of the 2E Unit. This staff re-organization allowed the 2B therapeutic recreation specialist more time to develop individual goals for each patient and maintain sterile recreation supplies specific to the interests and skills of each isolated patient. Also, with the cooperation and encouragement of the various medical teams, the therapeutic recreation staff in this program have become a more integral part in the research done on the Units (2E/2B).

### 2. Out-Patient Service (West Clinic)

Our involvement in programming for this service has grown by leaps and bounds. The therapeutic recreation program was designed to provide activities and services to outpatients, their families and guests. These activities helped fill many long and anxious hours of waiting and provided opportunities for the expression of fears, anxieties, hostilities, and fantasies.

An effort has been made to better serve the clinic patients and their families by the addition of specific games, supplies, and equipment geared to the needs of th patients and the space and medical restrictions of the clinic setting. One such useful addition has been the leasing of a portable Video Viewer which enables us to show cartoons and short movies to groups and individual outpatients on short notice and in small and/or atypical places. (i.e., in the treatment room while patients receive chemotherapy; in vacant examining rooms.)

The therapeutic recreation specialists in the clinic are being trained to retrieve information from the Clinical Center Medical Information System. This should better enable us to more rapidly obtain admission information which will enhance our ability to provide more consisten care and support to clinic patients who have been admitt to 2E/2B.

So that we may more consistently make the medical staff of the POB more aware of our patient observations and suggestions, and to properly document patient interactions, the clinic therapeutic recreation staff has been charting this information for several months. The information is recorded in the Daily Progress Notes section of the patient's chart.

The clinic therapeutic recreation staff attends several weekly meetings as a contributing part of the interdisciplinary team. These meetings include: 1) a multidisciplinary meeting during which all the disciplines working with Pediatric Oncology patients are represented and 2) a Social Work meeting which is composed of the Pediatric Oncology social workers, the clinic nursing staff, and the clinic therapeutic recreation staff. It has been suggested that the latter meeting be described in a paper to be presented at the 1980 Association for the Care of Children in Hospital Conference, and in various other appropriate professional organizations because of its unique characteristics.

### D. NICHD (9 West/D)

The patient population on this unit was very diverse, coming from six different Institutes. Our involvement included participation in the weekly interdisciplinary NICHD meeting, plus programming for all patients housed on the unit including the obsessive-compulsive mental health patients. Even though this Unit was classified as pediatric, the age range of patients fluctuated weekly from infant to middle-adolescent. The normal playroom activities were diverse enough to offer interesting programs for the younger patients; however, the adolescents on the unit required additional programming in order to meet their particular needs. Thus, the therapeutic recreation staff initiated a weekly planning meeting with the adolescents to involve them in the planning of weekly outings. The response from the adolescent patients was gratifying, and the medical staff was very supportive.

### E. NHLBI (Unit 7 East)

As a result of numerous referrals from Unit doctors, nurses, and social workers for recreation activities for their confined patients, a therapeutic recreation specialist was assigned, part-time, to provide recreation services to this Unit. A therapeutic program of creative crafts and social activities was implemented in order to meet the individual needs of each patient involved. The assigned therapist has become an integral member of the Unit research team, and the program has succeeded in meeting the recreational and emotional needs of patients and their families.

### F. NINCDS (Units 5 East/West)

#### Patient Council (Units 5E/W)

The therapeutic recreation program on these units continued to receive full support by a Patient Council - an informal group of patients and their relatives who met once a week to provide input into the recreation program. This Council provided an opportunity for patients to become better acquainted and to form supportive relationships, and to contribute their talents to the program.

#### Exercise Class

Under the direction of the Unit Therapeutic Recreation Specialist, a physician prescribed exercise program was initiated for these units. The classes met three times a week and mainly involved Parkinsonian and seizure disorder patients. The exercises were done either on the floor or in chairs and were designed to strengthen and add suppleness of movement. This program has had full support of nursing and physical therapy and, thus far, has been very well received by both patients and staff alike.

G. NIMH

Our therapeutic recreation program in this area changed its philosophical approach to serving the patients. This past year the staff functioned as a team to cover "core" programs designed for all mental health patients and openly encouraged intra-Unit participation in activities, while continuing their priority coverage of an assigned Unit. These changes increased programming opportunities and broadened communications among the Therapeutic Recreation staff, and other members of the Unit therapeutic milieu.

Charting

In order to properly document our patient programs and keep people informed of patient interactions, we began charting in the Professional Services Section of patient clinical records. Each Therapist initially interviewed the patient (with the primary nurse present when possibl and assessed his capabilities and strengths, setting up a recreation therapy plan. Weekly notes were made, with a discharge summary of recommendations being part of the plan. Patient future leisure plans were of primary importance to us, and these plans remain the ultimate goal for the Recreation Therapists in their work with the patient.

Research Protocols

For the past year, the recreation therapy program has been collaborating with two units on research protocols. On 2 West, the State Dependent Learning Protocol for Hyperactive Children has involved recreation therapy. Twelve hyperactive children were admitted under this protocol to measure the long term affects of dextroamphetamine. Criteria used in the study were activity ratings and behavorial ratings in gym, with rollerskates and basketball as the main source of activity. Cognitive testing was performed immediately after gym. This study and the accompanying data are now in the process of being written. The recreation therapist was responsible for taking the children to gym, keeping them as active as possible for a 45 minute period, as well as keeping accurate activity and behavorial ratings on each child. Ms. Patti Tepsic, the recreation therap is collaborating with Dr. Judith Rappaport on this paper. Ms. Tepsic has also been working with Dr.

Robert Post of 3 West on the Activity Exercise Lumbar Puncture study. Patients involved in this study arise at 2 a.m., at which time the recreation therapist provides certain high, moderate and low activities for a period of six hours. The patients must be kept busy the entire time, and afterward the physician performs a lumbar puncture. The purpose is to measure certain neurotransmitter metabolites in the cerebral spinal fluid which may affect mania. More patients will be involved in this study before the results can be published.

H. SACP (United Inn)

Our involvement in this program grew considerably over the past year. Patients at the Inn were serviced approximately 20 hours per week with a recreation program consisting of sightseeing and shopping trips, bingo games, movies, bowling, exercise classes, and special banquet-parties. These activities gave the patients and their families the opportunity to interact, unwind, and "get away from it all." The growth of this recreation program at the Inn has helped alleviate much of the isolated feelings of those patients who are housed outside the Clinical Center.

I. Wheelchair Program

The Adult Social Program staff initiated a series of activities specifically geared for wheelchair patients. These patients were visited and encouraged to participate in "outings" of their choice: to museums and other places of interest in the Washington area. The wheelchair trips were made possible through the rental of a special wheelchair van, although we hope to have our own van that will accommodate them in the near future. Since many wheelchair patients assume that they cannot be included in regular ambulatory activities, the initiation of this program has enabled them to get out of the hospital more frequently and to truly feel more a part of the Clinical Center patient population.

J. Patient Christmas Committee

The success of our patient Christmas program was not solely ours. The Patient Christmas Committee, made up of representatives from Nursing, American Red Cross, Social Work, Nutrition, R&W Association, Spiritual Ministry, CC Volunteer Office, and Executive Office, worked together to bring the most meaningful holiday experience to our patients. Specifically speaking, 31 trees were purchased by R&W for use throughout patient areas, 73 special gifts were purchased for emotionally and/or financially deprived patients, and approximately 120 token gifts were distributed on Christmas morning.

K. Student Fieldwork/Internship Program

We continued to be very involved in training students from various colleges and universities to help them meet their "final" undergraduate and graduate fieldwork requirements. We have become an accredited "Fieldwork Placement" agency with at least five schools. This year we had two seniors from the University of California, Sacramenta, Ca., one from the University of Maryland, one from the University of Indiana, Bloomington, Ind., and one from Virginia Polytechnical Institute & State University, Blacksburg, Va.

L. Unit Newsletters

In order to better communicate with patients in our bedside/unit programs, "newsletters" were put together by the various Unit therapists, with some patient help, in order to enhance the promotion of Unit, as well as Clinical Center-wide, recreation activities. Thus far, newsletters are successfully being published in the follo ing areas:

Unit 9D - - - - - - "Teen View"
SACP (United Inn)- - "The Newsletter"
NIMH (all units) - - "RecreAction"
Unit 10E - - - - - - "Mini-View"
Units 5E/W - - - - - "Fun on Five"

M. Patient Activity Schedule

In an attempt to improve the appearance and appeal of ou published weekly schedule of patient events, we have used a greater variety of colors, heavier and better quality paper, and more appropriate and creative pictures, as well as the inclusion of "special" quizzes and promotiona features ("Medicine for the Layman"). All of these have come about as the result of assigning a trained voluntee full-time to the preparation and circulation of this schedule (see below). Also, we made more of an effort to utilize patient art skills; most of our covers, and some incidental art work, were done by a very talented patient from Unit 5E. Response from all directions has been most favorable.

### N. Work Therapy Program

This past year, we had two mental health patients assigned to us as part of their work therapy and rehabilitation. Both patients worked in the Department office; one was assigned various clerical duties, and the other was trained in putting together our weekly patient activity schedule. In fact, after discharge, one patient became a volunteer and has continued his work with us (30 hours/week) on our schedule (see above); he has become an extremely valuable asset to the successful functioning our our Department's office.

## IV. PROFESSIONAL INVOLVEMENT OUTSIDE OF CLINICAL CENTER

### Maryland Recreation & Parks Association
### (Therapeutic Branch)

Executive Board Member - Sue O'Connell
Chairman, Nominating Committee - Arnold Sperling
Chairman, Constitution & By-Laws and Governance Committees- Sue O'Connell
Chairman, Professional Standards Committee - Cynthia Kauff
Chairman, Public Relations Committee - Holly Anderson

### Conferences/Meetings/Workshops

1978 National Congress on Recreation & Parks; Miami Beach, Florida, (Vera Sales, Sue O'Connell, Cynthia Kauff)

New Games Workshop, New Games Foundation; Columbia, Md. (Patti Tepsic, Cynthia Kauff)

Annual State Conference on Recreation and Leisure Services; Ocean City, Md. (Sue O'Connell, Cynthia Kauff)

Mid-Eastern Symposium on Therapuetic Recreation; Rutgers University, New Brunswick, New Jersey (Ron Hunt)

Annual Conference, Association for the Care of Children in Hospitals; Los Angeles, Ca. (Janis Partin, Patti Tepsic)

Workshop - Recreation and Its Feasibility in Correctional Institutions; MRPA, Nov. 1978 (Cynthia Kauff, Arnold Sperling, Sue O'Connell, Jane Millman, Cindy Pregent, Ron Hunt, Patti Tepsic)

98th Annual Conference, American Library Association; Dallas, Texas (Lois Swim)

Interpersonal Relations Workshop; NIH, Bethesda, Maryland, (Joan Vigersky, Patti Tepsic)

Other

Session on "Therapeutic Recreation - Professional Surviv
Annual State Conference on Recreation & Leisure Servic
Therapeutic Branch, MRPA, Ocean City, Md.
(Cynthia Kauff)

Therapeutic Recreation Management School; National
Recreation & Parks Association & the University of
Maryland; Oglebay Park, Wheeling, W.Va. (Arnold Sperli

## V. FUTURE OBJECTIVES

Continued emphasis in working with "special" patients on a one-to-one basis

Greater communication, both verbal and written, with other hospital disciplines and among our own staff

Continued development of a standard means of patient docum tation and evaluation

Incorporation into the Clinical Center Medical Information System

More involvement in the leisure counseling aspects of therapeutic recreation.

Therapeutic Recreation Section

Attachment #1

## 1. Adult Recreation Referral Program

| | Number of Referrals | Number of Referrals |
|---|---|---|
| NIAID | 843 | 517 |
| NIAMDD | 409 | 266 |
| NICHD | 131 | 65 |
| NCI | 591 | 409 |
| NEI | 82 | 49 |
| NHLBI | 805 | 519 |
| NINCDS | 181 | 94 |
| NIMH | 200 | 81 |
| SACP | 448 | 337 |
| Total | 3690 | 2337 |

## 2. Children's Play Program

| | Patients | Child Visitors | Total |
|---|---|---|---|
| NIAID | 41 | 7 | 48 |
| NIAMDD | 20 | 7 | 27 |
| NICHD | 236 | 8 | 244 |
| NCI | 120 | 88 | 208 |
| NEI | 23 | 0 | 23 |
| NHLBI | 52 | 14 | 66 |
| NINCDS | 25 | 14 | 39 |
| NIMH | 62 | 8 | 70 |
| SACP | 110 | 70 | 180 |
| Total | 689 | 216 | 905 |

## 3. National Institute of Mental Health

| | | |
|---|---|---|
| Unit 2 West | 202 | patients |
| Unit 3 East | 113 | patients |
| Unit 3 West | 113 | patients |
| Unit 4 East | 129 | patients |
| Unit 4 West | 110 | patients |
| Total | 667 | |

## 4. National Cancer Institute - Special Unit Program

| | | |
|---|---|---|
| Unit 10 East | 985 | patients involved |
| Unit 12 East | 521 | patients involved |
| Unit 12 West | 335 | patients involved |
| Unit 13 East | 607 | patients involved |
| Total | 2448 | |

## Patient Library Section

Attachment

### Reading Utilization

| Item | Number on Hand | Number Circulat |
|---|---|---|
| Stereo Record Players | 32 | 247 |
| Records | 654 | 3581 |
| Talking Book Machines | 5 | 19 |
| Talking Books | 57 | 25 |
| Magnifying Glasses & Bed Specs | 8 | 13 |
| Bookracks | 4 | 14 |
| Earphones | 7 | 26 |
| Cassette Players | 5 | 105 |
| Cassettes | 43 | 86 |

# ANNUAL REPORT 1978 -1979
# ANESTHESIOLOGY

## I. DEPARTMENT MISSIONS AND GOALS

The Anesthesiology Section, a division of Georgetown University Department of Anesthesia, is responsible for the clinical care of all patients requiring anesthesia and related clinical and research support services at the Clinical Center, the teaching of medical students, residents and other health personnel, and the development and continuation of a varied research program.

The goals of the division are:

1) To provide all patients at the Clinical Center with a trained anesthetist and medical consultant in the areas of surgical anesthesia, pain therapy, resuscitation and critical care.
2) To provide professional support to other divisions of the Clinical Center and the various Institutes in their investigational programs.
3) To initiate primary clinical investigations when opportune and appropriate.
4) To provide a teaching program for residents and medical students and other health personnel in the principles and clinical practice of anesthesia.
5) To participate in the continuing medical education program of the Clinical Center.

## II. DEPARTMENT ACTIVITIES

### CLINICAL

During the past twelve months, anesthesia and/or supportive treatment has been provided in 1667 instances, representing 1254 surgical operations, 347 diagnostic procedures, 27 nerve blocks, 29 consultations, and 10 resuscitations. Of these 131 were emergency procedures and 192 were open heart procedures requiring the techniques of extracorporeal circulation.

The accompanying tables indicate the distribution of patients according to sponsoring Institute and responsible surgical service (Table I); the distribution of anesthesia time by responsible surgical service (Table II); and the distribution of patients by anesthetizing location (Table III).

Analysis of these statistics indicates that the average length of a case is approximately 3.3 hours. Anesthesia support for the Hyperthermia Project of the NCI continues to be an integral part of the division's work. There were 96 hyperthermia cases during the past year with an average length of 6 - 7 hours per case.

TABLE I: DISTRIBUTION OF PATIENTS ACCORDING TO SPONSORING INSTITUTE AND RESPONSIBLE SURGICAL SERVICE

| SPONSORING INSTITUTE | DISTRIBUTION OF PATIENTS | | | |
|---|---|---|---|---|
| | SPONSORING INSTITUTE | | RESPONSIBLE SURGICAL SERVICE | |
| | # | % | # | % |
| NCI | 868 | 53. | 1116 | 69. |
| NHLBI | 387 | 24. | 348 | 21. |
| NINCDS | 98 | 6. | 98 | 6. |
| NEI | 5 | 0.3 | 4 | 0.2 |
| NIDR | 8 | 0.7 | 11 | 0.7 |
| NICHD | 39 | 2. | 9 | 0.6 |
| NIAMDD | 107 | 7. | - | - |
| NIAID | 64 | 4. | - | - |
| NIMH | 52 | 3. | 42 | 2.5 |
| TOTAL | 1628 | 100. | 1628 | 100. |

TABLE II: DISTRIBUTION OF ANESTHESIA TIME BY RESPONSIBLE SURGICAL SERVICE

| RESPONSIBLE SURGICAL SERVICE | TOTAL NUMBER CASES | AS A % OF THE TOTAL | 3 HOURS OR LESS | | OVER 3 TO 5 HOURS | | OVER 5 HOURS | |
|---|---|---|---|---|---|---|---|---|
| | | | # | % | # | % | # | % |
| NCI | 1116 | 69. | 689 | 62. | 217 | 19. | 210 | 19 |
| NHLBI | 348 | 21. | 142 | 41. | 77 | 22. | 129 | 37. |
| NINCDS | 98 | 6. | 49 | 50. | 11 | 11. | 38 | 39. |
| NEI | 4 | 0.2 | 4 | 100. | - | - | - | - |
| NIDR | 11 | 0.7 | 3 | 27. | 6 | 55. | 2 | 18. |
| NICHD | 9 | 0.5 | 7 | 78 | 1 | 11. | 1 | 11. |
| NIMH | 42 | 2.6 | 42 | 100. | - | - | - | - |
| TOTAL | 1628 | 100. | 936 | 57.5 | 312 | 19.2 | 380 | 23.3 |

TABLE III: DISTRIBUTION OF PATIENTS BY ANESTHETIZING LOCATION

| LOCATION | Patients |
|---|---|
| 1. Main Surgical Suite-Bldg 10 | 1024 |
| 2. X-Ray Dept. -Bldg 10 | - |
| 3. Cardiac Cath Lab-Bldg 10 | 7 |
| 4. Surgical Suite-Bldg 10A - Heart | 360 |
| 5. Surgical Suite-Bldg 10A - Neuro | 89 |
| 6. Cath Lab-Bldg 10A | 5 |
| 7. Dental | 5 |
| 8. Hyperthermia-Bldg 10-13th Fl | 96 |
| 9. Electroconvulsive Therapy 10-4W | 42 |
| SUBTOTAL | 1628 |
| 10. Other - Nursing Units (Intubations, Resuscitations, Consulations) | 39 |
| TOTAL | 1667 |

The Recovery Room, in its first full year of operation, admitted an average of 6 - 7 patients per day. Approximately 25% of all blood gases were performed by Recovery Room personnel. Utilization of the Recovery Room and Recovery Room personnel has exceeded anticipated goals.

## TEACHING

The second major activity of the Anesthesia Section is the teaching of medical students and residents. The department offered for the first time this year an elective to Third Year Medical Students in the Georgetown University Surgery Clerkship. Forty students participated in the two week elective at the Clinical Center. The basic format of the course includes a clinical demonstration, faculty tutorial and a self-teach audiovisual program. Participation in the didactic sessions has been extended to other students involved in the Clinical Center Preceptorship Program.

As part of the Department's Residency Program, rotations were provided at the Clinical Center for senior residents in cardiac anesthesia, major cancer surgery, research and pulmonary medicine.

The department continued to be actively involved in the provision of CPR training to the Clinical Center.

The Recovery Room nursing staff participated as instructors in a course provided for nurses on the Heart-Lung Service as part of the In-Service program of NHLBI.

## RESEARCH

The division continued to provide professional support to the various Institutes and divisions of the Clinical Center in the investigational programs. In addition the division continues active participation in the following protocols:

1) Effects of Chronic Electrical Stimulation of the Brain and Narcotic Analgesics on Human Responses to Noxious and Non-noxious Stimuli: Clinical and Experimental Evaluations (NIDR).
2) Effect on Whole Body Hyperthermia Combined with Adriamycin in Patients with Metastatic Sarcoma and Other Cancers (NCI).
3) Phase I - II Trial of Hyperthermia and Methyl CCNU in Malignant Melanoma (NCI).
4) Post-Thoracotomy Pain Study (NCI).

5) Elucidation of Basic Mechanisms of Taste: Transduction by Studying the Effects of Topically Applied Neuropharmacologically Active Drugs on Taste Acuity in Normal Human Beings (NIAID).

The following protocols are currently under development:

1) Alterations in Cerebrospinal Fluid Catecholomines in Response to Depth of Halogenated Anesthetics in association with the NIMH and NINCDS.
2) Changes in Cardiac, Cutaneous and Splanchnic Sympathetic Activity in Response to Surgical and Anesthetic Strains During and Post Open Heart Surgery for Coronary Artery Bypass Grafts or Valvular Replacements in association with the NHLBI and NIMH.

## III. MAJOR PROGRESS IN RESEARCH, SERVICES, TRAINING, AND DEVELOPMENT.

Significant changes noted in the clinical area have included: 1) an expanded use of Anesthesia support for Electroconvulsive Therapy by the National Institute of Mental Health; 2) an expanded use of the services offered through the department's Pain Service; and 3) and expanded use of Recovery Room personnel in the areas of medical audit, clinical care in the Operating Room and research support.

A significant development in the teaching area has been the development of the Third Year Elective for Medical students as outlined above. Student response to this program has been enthusiastic.

Another major teaching endeavor of the Department has been in the area of continuing medical education. Programs during the past year have included: 1) co-sponsorship of the First Annual Chesapeake Bay Area Anesthesia Conference in May 1979; 2) coordination of the Annual Scientific Meeting of the Maryland-DC Society of Anesthesiologists in November 1978; 3) Clinical Anesthesia Study Commission program presentation for the Maryland-DC Society of Anesthesiologists on September 25, 1979, and 4) presentation of a scientic exhibit on the Department's work in whole body hyperthermia at the Annual Meeting of the American Society of Anesthesiologists in October 1978 and the 53rd Congress of the International Anesthesia Research Society in March 1979.

In addition individual faculty lectured at a variety of educational programs as follows:

Kathleen C. Hittner, M.D.

IHSS, Department of Anesthesia, Children's Hospital, August 25, 1978

Idiopathic Hypertropic Subaortic Stenosis: a Medical, Surgical and Anesthetic Diagnostic Management Challenge, Surgical Grand Rounds, University of Vermont, September 14,1978

The NIH Experience in the Treatment of Pheochromocytoma, Department of Medicine Grand Rounds, University of Vermont, September 15, 1978

Anesthesia for IHSS, Bay-Cap Conference, Baylor University, November 8-10,1978

Hypothermia and Complete Circulatory Arrest, Department of Anesthesia, Children's Hospital, December, 1978

IHSS, Department of Anesthesia, Walter Reed Army Hospital, March 8, 1979

CPR, Maryland-DC Society of Anesthesiologists, April 28, 1979

Management of Pheochromocytoma, First Annual Chesapeake Bay Area Anesthesia Conference, May 10-12, 1979

Drugs Used in Resuscitation, TV Film-Nursing Inservice, Clinical Center NIH, July 1978

Intubation and Basic CPR, Arthritis Clinical Associates, Clinical Center NIH, November 1, 1978

CPR, Emergency Room, Georgetown University Hospital, November 21, 1978

Certification for Use of Esophageal Obturator, Fire House, NIH, December 20 and 27, 1978

Essential Drugs Used in CPR, Nursing Service, Clinical Center, NIH, January 31,1979; April 18, 1979

Esophageal Obturator, Nursing Service, Clinical Center, NIH, March 14-16, 1979

Esophageal Obturator Use, Occupational Medical Service, NIH, March 20, 1979

Prophylactic Digitalization-Pros and Cons, NHLBI Surgical Grand Rounds, NIH, March 23, 1979

IHSS, OR Nurses, Clinical Center, NIH, May 2, 1979

Stephen F. Kennedy, M.D.

Treatment of Reflex Sympathetic Dystrophy, Third Annual Seminar in Anesthesiology, Educational Council for Anesthesiology in New Jersey, November 4, 1978

Pain Clinic, National Association of O.R. Technician, December 6, 1978

Local Anesthetics in the Emergency Room. Emergency Room Grand Rounds, Georgetown University Hospital, July 19, 1978

Anesthesia for the Toxemic Patient, Obstetrics and Gynecology Grand Rounds, Georgetown University Hospital, January 3, 1979

Epidural Steroids, Neurosurgery Grand Rounds, Georgetown University Hospital, April 20, 1979

Facial Pain, Dental Research Club, Georgetown University, April 23, 1979

Undiagnosed Pain Syndromes, Physical Medicine and Rehabilitation Symposia, May 24-25, 1979

Patricia Emma, R.N.

The Pulmonary System and ABG's, In-Service Lecture, Heart-Lung Nursing Service, NHLBI, December 18, 1978

Eileen Pierce, R.N.

The Adult Cardiac Surgical Patient, In-Service Lectures, Heart-Lung Nursing Service, NHLBI, December 20, 1978

The Renal System, In-Service Lectures, Heart-Lung Nursing Service, NHLBI, December 20, 1978

In the past year research projects were completed in the following areas:

1) Anesthetic Management of Patients With Hyperaldosteronism
2) Hemodynamics and Blood Gas Changes with Whole Body Hyperthermia
3) Hyperthermic Potentiation of the Alpha-Adrenergic Blockade Induced by Droperidol
4) Changes in Hemodynamics and Catecholamine with Whole Body Hyperthermia
5) Acute Hyperthermic Potentiation of Adriamycin Cardiotoxicity
6) Innovar Modification of the Ventilatory Response to Extreme Hyperthermia in Man
7) Phase I Clinical Trial of Whole Body Hyperthermia
8) Effect of Thermally-Induced Respiratory Alkalosis on Erythrocyte 2,3, Diphosphoglyceric Acid Levels
9) Auriculo-Temporal Nerve Syndrome - Its Occurrence and Treatment in Combined Modality Cancer Patients

The following papers were presented at national anesthesia meetings and/or published as a result of this work:

PRESENTATIONS

1) Hanowell S. Hittner KC, Kim YD, Macnamara TE: Primary hyperaldosteronism: the syndrome and the anesthetic management. Presented at the Annual Meeting of the Southern Society of Anesthesiologists, Williamsburg, Virginia, March 29-31, 1979
2) Hittner KC, Lees DE, Macnamara TE: Current management of pheochromocytoma. Presented at the Annual Meeting of the Southern Society of Anesthesiologists, Williamsburg, Virginia, March 29-31, 1979
3) Hittner KC, Kennedy SF: Obstetrical and anesthetic management of the parturient with IHSS. Presented at the Annual Meeting of the Society for Obstetric Anesthesia and

Perinatology, Winston-Salem, North Carolina, April 5-8, 1979

4) Kim YD, Lees DE, Bull J, Whang-Peng J, Schuette W, Macnamara TE: Hemodynamic and blood gas changes with whole body hyperthermia. Presented at the Annual Meeting of the American Society of Anesthesiologists, Chicago, Illinois, October 21-25, 1978

5) Kim YD, Lees DE, Bull J, Whang-Peng J, Schuette W, Macnamara TE: Hyperthermic potentiation of the alpha-adrenergic blockade induced by droperidol. Presented at the Annual Meeting of the American Society of Anesthesiologists, Chicago, Illinois, October 21-25, 1978

6) Lees DE, Bull J, Whang-Peng J, Schuette W, Macnamara TE, Bynum G: Innovar modification of the ventilatory response to extreme hyperthermia in man. Presented at the Annual Meeting of the American Society of Anesthesiologists, Chicago, Illinois, October 21-25, 1978

7) Lees DE, Bull J, Whang-Peng J, Macnamara TE, Schuette W, Atkinson ER: Auscultatory confirmation of esophageal temperature probe placement. Presented at the Annual Meeting of the American Society of Anesthesiologists, Chicago, Illimois, October 21-25, 1978

8) Lees DE, Hanowell S. Macnamara TE: Auriculotemporal syndrome: Its occurrence and treatment in the combined modality cancer patient. Presented at the Annual Meeting of the Southern Medical Association, Atlanta, Georgia, November 13, 1978

9) Lees DE, Emma P, Hittner KC, Kim YE, Macnamara TE: The safety of ketamine in pediatric neuromuscular disorders: a study of one hundred patients. Presented at the 53rd Congress of the International Anesthesia Research Society, Hollywood, Florida, March 11-15, 1979

10) Macnamara TE: The effect of thermally-induced respiratory alkalosis on erythrocyte 2,3, DPG levels and hemoglobin P50 determinations. Discussor, 53rd Congress of the International Anesthesia Research Society, Hollywood, Florida, March 11-15, 1979

11) Owens SW, Schuette W, Bull JM, Lees DE, Thibault L Whang-Peng J: The effect of thermally-induced respiratory alkalosis on erythrocyte 2,3, DPG levels and hemoglobin

P50 determinations. Presented at the 53rd Congress of the International Anesthesia Research Society, Hollywood, Florida, March 11-15, 1979

PUBLICATIONS

1) Bynum GD, Pandolf KB, Lees DE, et al: Induced hyperthermia in sedated humans and the concept of critical thermal maximum. Am J Physio: Regulatory Integrative Comp Physiol 4(3):R228-R236, 1979

2) Bull JM, Lees DE, Schuette W, et al: Whole body hyperthermia: A phase I trial of a potential adjuvant to chemotherapy. Ann Int Med 90:317-323, 1979

3) Hanowell S, Lees DE, Macnamara TE: Auriculotemporal syndrome after combined modality therapy for cancer. South Med J (in press)

4) Hanowell ST, Kennedy SF: Phantom tongue pain: Case presentation and treatment. Anesth Analg (in press)

5) Kim YD, Lees DE, Lake CR, Whang-Peng J, Schuette W, Smith R, Bull J: Hyperthermia potentiates doxorubicin-related cardiotoxic effects. JAMA 241:1816-1817, 1979

6) Kim YD, Lake CR, Lees DE, et al: Hemodynamic and plasma catecholamine responses to hyperthermia treatment of metastatic cancer in humans. Am J Physio (in press)

7) Kim YD, Hittner KC, Lees DE, et al: Vasodilator correction of hypotension in the postoperative period: A case report. South Med J (in press)

8) Lees DE: Book review. Second International Symposium on Malignant Hyperthermia. Anesthesiology 49:444-445, 1978

9) Lees DE, Schuette W, Bull JM, et al: Evaluation of liquid crystal thermometry as a screening device for intraoperative hyperthermia. Anesth Analg 56:669-674, 1978

10) Lees DE, Kim YD, Schuette W, et al: Causes of induced hyperthermia (letter). Anesthesiology 50:69-70, 1979

11) Lees DE, Kim YD, Schuette W, et al: Auscultatory confirmation of placement of esophageal temperature probe. Anes Rev (in press)

12) Owens SW, Atkinson ER, Lees DE: Thermographic evidence of reduced sympathetic tone with stimulation. Anesthesiology 50:62-65, 1979

13) Schuette WH, Lees DE, Bull JM, et al: Feedback control of esophageal temperature during whole body hyperthermia, 1978 Advances in Bioengineering, edited by RC Eberhart and AH Burstein, New York, American Society of Mechanical Engineers, 1978, pp109-111

14) Savage TM, Dubois M, Frank M, Holly JMP: Preliminary investigation into a new method of assessing the quality of anaesthesia: the cardiovascular response to a measured noxious stimulus. Br J Anaesth 50:481-488,1978,

15) Dubois M, et al: Recovery from anaesthesia, Br J Anaesth 50:825-832, 1978.

16) Johnpulle CJR, Macnamara TE: Respiratory intensive care nursing. In: Brunner LS and Suddarth DS (eds): Textbook of Medical-Surgical Nursing, ed. 4, (in press).

## IV. FUTURE OBJECTIVES

The principle objective of the Department continues to be the provision of appropriate anesthesia support to patients of the Clinical Center. In particular, in the coming year department efforts will be focused on the expansion and upgrading of the neuroanesthesia service at the Clinical Center in conjunction with the expanded work of the National Institute of Neurological and Communicative Disorders and Stroke.

In addition departmental efforts will be focused on the following special areas of interest:

1. Participation in the Medical Student Elective Program of the Clinical Center.
2. Development of a research support program in the department to assist the anesthesiologist with clinical investigations.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>ANES<br>Z01-CL-07005-02 ~~NCR~~ |

PERIOD COVERED
October 1, 1978 - March 30, 1979

TITLE OF PROJECT (80 characters or less)
Prevention of Post-Thoracotomy Pain by Bupivicaine (Marcaine) Nerve Block Anesthesia

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Eugene Woltering, MD | Clinical Associate | Surgery Branch, DCT, NCI |
| Other: | Phillip Kapp, MD | Attending Anesthesiologist | Anesthesiology Section |
| | M. Wayne Flye, MD | Senior Investigator | Surgery Branch DCT, NCI |

COOPERATING UNITS (if any)
NCI, CC

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 1.5 | |

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Post Thoracotomy pain patients were divided into three groups: one reviewed inter costal block with Marcaine in OR prior to closing the chest incision; one group had polyethylene catheters inserted in OR prior to chest closure for administration of Marcaine at six hour intervals postoperative; the third group served as a control group receiving narcotic sedation as ne for postoperative pain. Narcotic sedation was also used in both Marcaine groups if needed for additional pain relief.

Preliminary results, still pending further analysis of data, seem to indicate:

1) There was no significant difference in the amount of MS used for postoperative pain relief in any group.
2) Although observers thought the Marcaine groups performed postoperative pulmonary function tests better than the control group, there was no statistical difference in any of the groups with regard to pulmonary function studies or arterial blood gases postoperatively.

PHS-6040
(Rev. 10-76)

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space)

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
**NOTICE OF INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER
Z01-CL-07004-02 ~~CM~~ ANES

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Pilot Study Examining The Effect of Whole Body Hyperthermia Combined With Adriamycin in Patients With Metastatic Sarcoma and Other Cancers

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Joan Bull, MD | Senior Investigator | COP, DCT, NCI |
| Other: | J. Whang-Peng, MD | Senior Investigator | COP, DCT, NCI |
| | William Schuette | Chief, ACE | BEIB, DRS |
| | David E. Lees, MD | Deputy Chief, Anes. | Anesthesiology Section |

COOPERATING UNITS (if any)
NCI
Anesthesiology Section
Nursing, Clinical Center
BEIB, DRS

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: 4
PROFESSIONAL: 4
OTHER:

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Following phase I studies of whole body hyperthermia alone in the treatment of metastatic cancer, selected patients with sarcomas or other solid tumors were begun on a protocol combining adriamycin administered at 41.5 C with two hours of hyperthermia in excess of 41.5 C. Initial dosage was 10 mg/m$^2$ with escalation as subsequent patients entered the protocol.

The intercurrent administration of adriamycin (doxorubicin) and hyperthermia has not been fully evaluated yet for its tumoricidal potential, but there is evidence of acute synergistic toxicity in several patients. The combined use has been associated with conduction disturbances, arryhthmias and increased liberation of endogenous catecholamines. Clinical experience has shown conventional antiarrhythmia therapy to be effective. These results were first published by the Anesthesiology Section in JAMA 241:1816-1817, 1979.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER |
|---|---|---|
| | | ANES<br>Z01-00784-01 ~~NAB~~ |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Effects of Narcotic and Brain Stimulation Analgesia on Human Chronic and Experimental Pain

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Richard Gracely, Ph.D. | Research Psychologist | NAB, NIDR |
| Other: | Ronald Dubner, DDS, Ph.D. | Chief | NAB, NIDR |
| | Raymond Dionne, DDS, Ph.D. | | NAB, NIDR |
| | Marvin Hoffert, MD | | NAB, NIDR |
| | David E. Lees, MD | Deputy Chief | Anesthesia Sec |
| | Peggy Amato, RN | | NAB, NIDR |

COOPERATING UNITS (if any)
NAB, NIDR
Anesthesiology Section

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 8 | 8 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purposes of this study are threefold: (1) Assess the effectiveness
chronic electrical stimulation of midbrain sites for the relief of chronic pa
in humans; (2) Evaluate the efficacy and mechanisms of traditional narcotic
analgesia and compare these to that found for chronic electrical stimulation
midbrain sites; and (3) Validate experimental models of pain and their poten
diagnostic use in chronic pain patients. In addition, this study will deter
and compare the impact of both traditional narcotic and chronic electrical
stimulation therapies on the functional, intellectual and emotional well bein
of these patients. Three types of participants in this study will be chronic
pain patients who will receive surgically implanted stumulating electrodes fo
pain control, chronic pain patients maintained on traditional narcotic
analgesics who will not receive implanted stumulating electrodes, and healthy
normal volunteers. The effects of chronic brain stimulation in surgical
patients will be compared to the effects of narcotics previously administere
these patients and to effects of narcotic regimes in nonsurgical chronic pain
patients.

PHS-6040
(Rev. 10-76)

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-07001-02 ~~LBV~~ ANES |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Elucidation of basic mechanism of taste transduction by studying the effects of topically applied neuropharmocoligically active drugs on taste acuity in normal human beings.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Carl Mattern, MD | Assistant Chief, LVD | NIAID, NIDR |
| Other: | Phillip Kapp, MD | Attending Anesthesiologist | Anesthesiology Section |

COOPERATING UNITS (if any)
NIAID, NIDR

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 2.0 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Stage I - testing the effect of an oral application of Succinylcholine on a volunteer to demonstrate the safety of the procedure and to determine the effect of taste. The starting dose was 2.5 mg in 5 ml water. It was increased to 20 mg in 5 ml water. There was no significant effect on taste sensation at these doses.

The project is now pending reassessment of protocol and approval to use larger doses of the test drug.

PHS-6040
(Rev. 10-76)

NUCLEAR MED.
BLOOD BANK
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ESCD
DIAG. RADIOL.

(DO NOT use this space)

HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
**NOTICE OF**
**INTRAMURAL RESEARCH PROJECT**

Z01-CL-07003-02-~~CM~~
ANES

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

A Phase I - II Trial of Hyperthermia and Methyl CCNU in Malignant Melonoma

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Joan Bull, MD | Senior Investigator | COP, DCT, NCI |
| Other: | J. Whang-Peng, MD | Senior Investigator | COP, DCT, NCI |
| | William Schuette | Chief, ACE | BEIB, DRS |
| | David E. Lees, MD | Deputy Chief, Anes. | Anesthesiology Sec |

COOPERATING UNITS (if any)
NCI
Anesthesiology Section
Nursing, Clinical Center
BEIB, DRS

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>4 | PROFESSIONAL:<br>4 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The protocol has been modified such that methyl CCNU, an oral preparatio is no longer being used; BCNU, an intravenous agent, has been substituted. This was necessary since an efficacious drug level could not be demonstrated with the oral preparation and it was difficult to administer to a deeply sed patient during hyperthermia. The intravenous preparation has shown a greater clinical response and permits a smoother treatment course.

Critical Care Medicine Department, Clinical Center

## I. Department Missions and Goals

The Critical Care Medicine Department was established in November 1977 to care for critically ill patients throughout the Clinical Center who have potentially reversible medical problems. Critical care medicine may be defined as the observation, diagnosis, treatment, and rehabilitation of patients with overt or potential failure of vital functions.

The need for critical care medicine services has increased because of the gradual extension of clinical investigation to patients who are critically ill with potentially reversible medical problems. The Department is responsible for the respiratory therapy and physiological monitoring services frequently needed by critically ill patients. The Department is currently composed of the following administrative sections:

1. Clinical consultative services
2. Critical care unit
3. Physiological monitoring
4. Respiratory therapy

The function of the Department is to (a) provide optimal care for Clinical Center patients who may benefit from careful nursing observation to those patients requiring the application of one or more major life support systems, (b) work to improve both understanding and prevention of acute problems which frequently necessitate the need for critical care and (c) develop the best possible equipment, techniques, and systems for the management of the critically ill.

The activities of the Department have been directed principally towards:

1. Organizing and developing a department capable of providing a full spectrum of critical care services to the Clinical Center.
2. Designing, organizing, and constructing a critical care unit which will be readily accessible and easily utilized by any Clinical Center physician.
3. Developing a consultative service to assist in the management and care of critically ill patients throughout the hospital.
4. Developing and presenting an educational program for technicians, nurses, and physicians interested in critical care medicine.

## II. Department Activities

A. Clinical Consultative Service. Since its formation the Department has provided consultative service directed toward all aspects of the management of the critically ill patient. Detailed assistance in the evaluation of patients and institution of respiratory and hemodynamic life support systems have been provided; patients have been followed throughout that phase of their illness requiring life support measures. The consultative service is available on a twenty-four hour a day basis, seven days a week.

B. Critical Care Unit. The critical care unit occupies the 10-D wing on the 10th floor. The first patient was admitted on April 30, 1979. An automated data collection system designed t facilitate hour to hour and day to day management of the patien is now in use. In addition, this system provides for the stora of archival data to facilitate subsequent clinical investigatio A vascular research console has been designed to facilitate the detailed assessment of the hemodynamic status of patients and t permit vascular diagnostic studies to be performed on critica ill patients.

Three technicians have joined the staff with the Chief Technicia for the Critical Care Unit.

C. Physiological Monitoring Section. This section, consisting of a Chief, and three technicians, supplies, operates, and maintains physiological monitoring equipment utilized throughout the Clini Center. This includes the telementry of ECG signals, and the measurement of respiratory and vascular parameters both at the bedside and within the recovery room and intensive care units throughout the Clinical Center. This service is provided from 7 AM until 12:30 AM, Monday through Friday, and on an On Call basis at all other times. A summary of the services is listed in Table 1.

D. Respiratory Therapy Section. This section provides a full spec of respiratory therapy services (intermittent, positive pressure breathing, ultrasonic nebulization, incentive spirometry, oxygen therapy, chest physiotherapy, and mechanical ventilation), for al Clinical Center patients. This section also provides, as an adjunct service, blood gas determinations for the Anesthesia Recovery Room and for one of the research projects sponsored by the National Cancer Institute. Respiratory therapy services are available on a twenty-four hour a day basis, and the staff coverage is provided by the Chief, ten full-time technicians, and one part-time technician. A summary of this section's activities is presented in Table II.

## III. Major Progress in Research, Training and Development

With the invaluable assistance of the Laboratory of Computer Sciences of the Division of Computer Resources and Technology, an automated data collection system has been programmed to provide real time to collect all data for flow sheet generation. These protocols were developed, written, and debugged prior to the opening of the unit on April 30, 1979, which emphasize management of specific problems likely to be encountered within the Critical Care Unit.

Training of critical care technicians, nurses, and physicians interested in critical care medicine has been instituted through formal courses offered by FAES.

Three senior physicians have now joined the staff of the Critical Care Medicine Department:

> Joseph R. McClellan, M.D., formerly Chief of Cardiology, Berkshire Medical Center, Pittsfield, Massachusetts.
>
> Norman E. Adai ., M.D., formerly of the Pulmonary Medicine Department, University of Manitoba, Winnipeg, Manitoba, Canada.
>
> Robert M. Lester, M.D., formerly a Cardiology Fellow, Duke University Medical Center, Durham, North Carolina.

Dr. Byron B. McLees, Chief, Critical Care Medicine Department, Clinical Center, holds a Ph.D. in Physiological Chemistry, formerly Chief, Division of Pulmonary Medicine and Director, Intensive Care Unit, Durham Veteran's Administration Hospital, Durham, North Carolina, and most recently, Expert Consultant, Pulmonary Branch, NHLBI, NIH.

## CRITICAL CARE MEDICINE DEPARTMENT

### TABLE I

| BLOOD GAS ANALYSIS | | OXYGEN THERAPY | RESPIRATORY THERAPY TREATMENTS IPPB | | AEROSOL | | CHEST PHYSIO-THERAPY | | MECHANICAL VENTILATION | |
|---|---|---|---|---|---|---|---|---|---|---|
| TOTAL | | TOTAL PATIENTS | TOTAL | | TOTAL | | TOTAL | | TOTAL | |
| PTS. | NO. | | PTS. | TXS. | PTS. | TXS. | PTS. | TXS. | PTS. | HRS. |
| 318 | 1909 | 1143 | 220 | 2057 | 453 | 4173 | 385 | 2,000 | 165 | 33,331 |

### TABLE II

### PHYSIOLOGICAL MONITORING SECTION

| INTRA-VASCULAR MONITORING (Arterial & Venous Pressures, and Pulmonary Artery Pressures) | NON-INVASIVE MONITORING (ECG-Heart Rate, Radio Telemetry, Respiration and Temperature) |
|---|---|
| TOTAL NUMBER OF PATIENTS | TOTAL NUMBER OF PATIENTS |
| 1175 | 1573 |

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DIAG. RADIOL.

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE: NATIONAL INSTITUTES OF HEALTH

## SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES CLINICAL CENTER

## BLOOD BANK DEPARTMENT:

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II Department Activities BB- 2

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- B. Department Organization BB- 4
- C. Donor Program BB- 4
- D. Laboratory Service BB- 4
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5. Chronic Sequelae of Non-A, Non-B Hepatitis. BB-29

6. The Duffy Blood Group Determinant and Susceptibility to Malaria. BB-32

7. Chido ($Ch^a$) Antibody Production Induced by Cancer Immunotherapy. BB-36

8. Mechanism of Vertical Transmission of Hepatitis B Virus. BB-39

9. Transmission of Non-A, Non-B Hepatitis in Chimpanzees. BB-42

10. Evaluation of Anti-Core Antibody and Serum Transaminase as Indicators of the Infectivity of HBsAg-Negative Donors. BB-45

11. Identification of the Non-A, Non-B Hepatitis Agent and the Development of Serologic Markers. BB-48

12. Hepatitis B Vaccine Trial Among Renal Dialysis Patients. BB-51

13. Evaluation of the Hepatitis Risk of Hospitalized Patients Undergoing Invasive Procedures, but Not Receiving Blood Transfusion. BB-54

14. Alterations in Whole Blood Oxygen Affinity Following Transfusion. BB-57

15. Identification of Bacterial Organisms with Red Cell Antigen Specificity. BB-60

16. Blood Group Substances in Malignant and Benign Breast Cyst Fluids. BB-63

17. Frozen Red Cells in the Prevention of Non-A/Non B Hepatitis. BB-66

18. Chronic Transfusion with a Fraction of Young Normal Red Cells (Neocytes). BB-69

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October 1, 1978, through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## BLOOD BANK DEPARTMENT

### I. BLOOD BANK MISSIONS AND GOALS

The Blood Bank Department sees itself as a unique facility in a unique health care organization. While the Department provides the entire range of service responsibilities commonly encountered by blood banks at other institutions, we are frequently challenged by unusual service demands. In addition, we are stimulated by the teaching and research activities as well as opportunities which have come to be associated with the National Institutes of Health.

We consider our primary mission to remain the provision of an adequate supply of high-quality, safe blood and blood products to Clinical Center patients. It is upon this primary commitment to patients that the other goals and activities of the Blood Bank are based. In order to ensure that these service responsibilities are met in the most professional, timely, and economical manner, several service-related goals have been established for our Department.

The demand for specialized blood components for Clinical Center patients is increasing. Thus, one goal is to increase our professional and technical expertise in component preparation and therapy by taking advantage of the newer technical advances in the science of component preparation; demands for special blood products will then not only be expeditiously met, but will be will be anticipated and planned for. Another goal is to increase our patient care consulting capacity in the expanding field of immunohematology and hemotherapy. An additional goal related to our service mission is to continue to expand our blood donor base on the NIH campus and in our off campus buildings. It is primarily through reliance on our fellow NIH employees that we feel our blood and component supply needs can be most effectively and economically met. A further service goal is to expand our activities in testing, introducing, and incorporating new laboratory techniques and procedures related to blood banking. This requires a number of cost saving measures but allows accommodation of increased functions without sacrficing patient safety or welfare.

A second mission of the Blood Bank Department is to maintain an active teaching program in the disciplines of immunohematology and blood transfusion. Formal training programs exist in the Department for medical technology students, for registered technologists who are specializing in blood banking, for clinical pathology resident physicians, and for physician fellows specializing in blood banking. In addition, informal training experiences are available for visiting scientists and physicians. Our goal related to this training mission is to maintain and improve our teaching programs so that we continue to attract and train candidates of the highest caliber.

The Blood Bank staff also feels a responsibility to teach area medical students, nurses, technologists and physicians in addition to our "in-house" training programs. Active faculty positions are maintained at Georgetown, George Washington, Johns Hopkins, and the Uniformed Services Medical Schools. Courses are taught to students in the FAES Graduate School at NIH, and to Clinical Center nurses who are learning the nursing skills related to blood transfusion. Our goals are to continue our teaching commitment to the professional community in our hospital, as well as at other local professional centers, and to improve these activities as necessary.

The emphasis placed on the research mission of the Clinical Center Blood Bank (CCBB) is one of the strengths of our organization. It is clear that our position as the Blood Bank of the National Institutes of Health, our past record of research contributions, and the varied research interests of our staff raise research to a high priority in our hierarchy of goals. Contributions continue to be made in our traditionally strong research areas of viral hepatitis and immunohematology. In addition, new research initiatives are being carried out in innovative application of pheresis and hemotherapy, and, in the near future, HLA research and tissue typing. Our goal is to maximize the potential for creative research which exists in our staff, to share our research findings with the rest of the professional community through publications and presentations, and to continually strive to secure new and constructive advances in our field.

The three primary missions of the Clinical Center Blood Bank remain service, teaching, and research. Through the goals outlined above, we anticipate fulfilling these missions successfully, competently, and confidently. More specific objectives related to these goals will be found in Section IV.

## II. DEPARTMENTAL ACTIVITIES

### Service Responsibilities

More than 8000 units of whole blood and red cells were transfused during the past year, a 5% increase over the previous year. Approximately 65% was drawn in our own blood bank, with the remainder supplied primarily by the Washington Regional Red Cross Blood Program. While still not self sufficient, provision of 65% of NIH's blood needs represents a major improvement from last year (51%).

The Blood Bank increased production of fresh frozen plasma 10 fold, now approximately 100 units per month. For the first time we produced more than Clinical Center patients consumed. The balance was exchanged with local hospitals for other components needed by Clinical Center patients; this helped the general, regional supply of plasma. Sufficient cryoprecipitate was prepared to meet the needs of all Clinical Center patients; and, in one instance, enough single donor cryoprecipitate was stockpiled by means of pheresis procedures to permit major surgery on a patient with dysfibrinogenemia. Like last year the out-patient hemophilic patients were supplied by factor VIII commercial concentrate acquired both by direct purchase and by exchange for outdated plasma.

Blood Bank physicians continued to perform clinical consultations on patients with immunohematological problems and suspected viral hepatitis after transfusions. For example, more than 70 reported transfusion reactions were evaluated, two thirds of these were in fact transfusion related. Blood Bank consultants were active in evaluating intraoperative coagulation problems. They helped evaluate an automated system for monitoring heparin use during open heart surgery, a technique which promises to decrease the need for blood and blood products.

The Blood Bank assumed a more active role in therapeutic procedures during the past year. Numerous manual phlebotomies were performed on patients with polycythemia and hemachromatosis. The addition of a second cell separator, the IBM 2997, enabled us to perform approximately 10 therapeutic procedures per month, including plasma exchanges in patients with systemic lupus erythematosis, Waldenstrom's macroglobulinemia, and hyperlipoproteinemia. Additional automated red cell exchanges in sickle cell patients were completed, giving us the greatest reported experience with this procedure in the world. Approximately 25 cell separation procedures are now performed each month.

The Plateletpheresis Center, in its sixth year on an NCI contract, continued to function at close to maximum capacity. The Center recruited more than 3500 donors and performed more than 3300 four-unit manual plateletphereses. The Blood Bank monitored its performance. In addition, we produced 15% of the platelets used by Clinical Center patients from single donor units and automated pheresis, an increase of 400% over the previous year.

The Blood Bank continued to meet an increasing number of requests for blood products from the NIH "research community." We performed more than 30 manual plasmapheresis and fifteen automated pheresis procedures per month for research. Approximately 350 blood samples per month were drawn in the Blood Bank for NIH laboratory studies. Often, specialized methods of collection and preservation were required. In addition, we occasionally provided blood products for other government facilities, such as the provision of two liters of recovery phase plasma from a patient exposed to P. ovale malaria and one liter of plasma from several patients who had recently recovered from tularemia. These products were used for research purposes by the Center for Disease Control in Atlanta.

The Blood Bank immunohematology reference lab continued to investigate difficult erythrocyte serologic problems referred by physicians in area hospitals and throughout the country. Approximately 72 such problems were investigated over the past year. The elucidation of these cases has not only served the referring laboratory, but has provided excellent source material for teaching and for additional investigation.

## Department Organization

The Blood Bank Organization Chart is on page 20. Ms. Laurene Kolasinski was appointed Assistant Technical Supervisor of the laboratory area upon the resignation of Ms. Sandra Maytag. Ms. Betty Colbert assumed responsibility for supervising the Donor Recruiting Unit. A pheresis unit was established within the Blood Services Section and is currently staffed by one full-time nurse, one part-time nurse and one part-time research technologist.

## Donor Program

The Blood Bank continued its policy of using all volunteer blood. Current donor rolls stand at 2510, an all time high. On campus, the Blood Bank continued recruitment drives and offered free blood typing. Off campus, joint mobile operations with Red Cross were conducted at the Westwood, Landow, Federal, and Blair Buildings. For the first time in many years the Blood Bank conducted an independent mobile drive at NIH's Poolsville campus; this drive was successfully repeated twice more during the year. Blood Bank staff assisted a Clinical Center patient who elected to use donor recruitment as his Eagle Scout community service project; the result was more than 100 units collected on three Saturday sessions and an unexpected television news promotion for blood donation.

Despite a rift between the major national blood suppliers, the NIH Blood Assurance Program continued to run smoothly. Relatives of NIH employees received more than 450 credits or actual units of blood across the country.

## Laboratory Service

The Blood Bank Laboratory, divided into Compatibility Testing and Donor Processing areas, continued to provide 24 hour service, seven days a week utilizing extended hours of operation and an "on call" system. During the past year the laboratory staff determined the blood group and type of 3972 patients, performed 5439 direct Coombs tests, 6948 patient screening tests for irregular antibodies, and 11,090 crossmatches.

The "routine" laboratory work once again succeeded in the solution of far from "routine" problems. The staff identified five or more antibodies in the serum of several patients and was instrumental in identifying a previously unrecognized clinical syndrome in sickle cell patients who developed delayed hemolytic transfusion reactions. The laboratory staff also documented a hemolytic transfusion reaction due to an anti-$P_1$, an antibody generally regarded as being of little clinical significance.

During the past year, the Blood Bank assumed responsibility for processing and issuing granuloctye concentrates collected by NCI. All blood products collected at NIH for patient use are now processed and issued by the Blood Bank. In addition, irradiation of blood products for patients with compromised immune function is now a Blood Bank service. This was taken over from the NCI Pediatric Oncology Unit.

## Professional Activities

The professional staff has continued to participate actively in a wide variety of local, national and international meetings and programs during the past year.

Dr. Paul V. Holland travelled to the USSR again as a consultant for the NHLBI Scientific Exchange Program. He continued to serve on the Technical Manual Committee of the American Association of Blood Banks, on the American Red Cross Research Review Committee, as Chairman of the NHLBI Policy Board for the Transfusion Transmitted Viruses Study, and on various standing and ad hoc committees at NIH. He was active on the clinical faculty of the George Washington, Georgetown, and Uniformed Services medical schools. He lectured frequently at area hospitals and directed the FAES course, Immunology 508M.

Dr. Harvey J. Alter was chairman of the Scientific Working Group of the NIH Viral Hepatitis Coordinating Committee and was selected as a member of the Clinical Research Subpanel Committee for NIAID. He spoke widely on hepatitis, including the Third Scientific Lecture at the American Association of Blood Banks Annual Meeting, a lecture at the American Public Health Association Annual meeting, and the Annual Alumni Lecture at the University of Rochester School of Medicine. He was a member of the Medical Advisory Committee of the American Red Cross and a member of the Scientific Program Committee of the American Association of Blood Banks. Dr. Alter is clinical associate professor of medicine at Georgetown University Hospital. He made numerous presentations to NIH groups and area hospitals and was a faculty member of the FAES course, Immunology 508M.

Dr. Harvey G. Klein continued as a consultant to the Johns Hopkins Hospital in the Hematology Clinic and was a speaker at hematology and clinical pathology grand rounds there. He was appointed chairman of the Regionalization Committee of the Metropolitan Washington Blood Bank Association and was a participant on the Regionalization Meeting of the Council of Community Blood Centers in Scottsdale, Arizona. He spoke at the Center for Blood Research in Boston and at the Milwaukee Blood Center. He continued as a member of the NIH Hemophilia Review Committee, MCHS, HSA. He continued as attending physician for Clinical Hematology (NHLBI), and was on the faculty of the Uniformed Services Medical School, and was a faculty member of the FAES course, Immunology 508M, and the Nursing Department's blood transfusion course.

Dr. Richard J. Davey is clinicial assistant professor of medicine at Georgetown University Hospital; he served as attending physician for the Department of Medicine, as instructor for the second year medical school course in hematology, and as a speaker at the Georgetown hematology conference. He spoke at the Department of Pathology rounds at Providence Hospital and at the University of Virginia. He was a member of the NIH Clinical Center Education Coordinating Committee and coordinator of educational activities in the CCBB. He was a faculty participant in the USUHS pathology course and the FAES sponsored Immunology 508M. For the Nursing Department's blood transfusion courses which trained 217 CC nurses this past year, he was the coordinator for the Blood Bank teaching effort and one of the lecturers.

Ms. Mary H. McGinniss continued to serve on the Scientific Section Coordinating Committee, the Scientific Program Committee, and the Standards Committee for the American Association of Blood Banks. Ms. McGinniss conducted numerous teaching sessions in immunohematology throughout the year, was a guest lecturer in Immunology 508M, and participated in the Clinical Pathology Department conferences. Ms. McGinniss was an invited guest speaker at the Ohio State Blood Bank Meeting in Cleveland and the Mid Atlantic Association of Blood Banks Meeting in Virginia.

Laboratory supervisor, Ms. Mary Gustafson, continued to serve on the advisory committee for the Montgomery College MLT program and as preceptor for the Blood Bank rotations at NIH. Ms. Gustafson continued as Education Coordinator for the Specialist in Blood Banking (SBB) students and is currently on the faculty of Immunology 508M.

Ms. Laurene Kolasinski became certified as a Specialist in Blood Banking (SBB).

Ms. Janice Sigmon served as secretary of the Society of Hemopheresis Specialists.

## Honors and Awards

Dr. Paul Holland received the USPHS Meritorious Service Medal; the citation read, "For excellence as a teacher of immunohematology, as a hepatitis researcher, and as a leader of a blood bank recognized widely for service, teaching and research." He also received a Silver Medal from the National Institute of Hygiene, Warsaw, Poland for his collaborative research studies with this institution.

Ms. Betty Colbert received a special citation from the Secretary of H.E.W. for being one of the Ten Outstanding Employees of the Year of D.H.E.W.

The Secretarial Staff, Ms. Betty Colbert, Ms. Lucille Kilmain, Ms. Barbara Orr and Ms. Phyllis Thomas, received a Group Award for their continuous Superior Performance.

Ms. Rachael Solomon received a Quality Increase Award for her continuous, outstanding work.

Ms. Anna Brown received a Ten Years of Service Award.

Mr. Dana James received an Award for his Sustained Superior Performance.

The Blood Bank Department was voted first among Clinical Center services in a poll of Clincial Associates. This is the second year in a row the Department has been so honored.

## III MAJOR PROGRESS

### Hepatitis

The Blood Bank continues to investigate the frequency, etiology, and prevention of post-transfusion hepatitis (PTH). The final serologic tests are now being completed on the largest prospective study of PTH ever undertaken by the BBD. Over 500 patients and 150 controls have now completed nine months of intensive follow-up after open heart surgery (patients) or cardiac catheterization (controls). The non-transfused control population is an innovation in these ongoing studies. The final analysis is not complete, but it appears that, despite the exclusive utilization of volunteer donors screened by a sensitive radioimmunoassay for HBsAg, approximately 8% of this multitransfused patient population continues to develop evidence of PTH. Almost 95% of the PTH is classified as non-A, non-B. There have been no cases of type A PTH and there have been no cases of type B hepatitis in the past two years (3 cases were found in the first year of the study). Approximately 1% of non-transfused patients also develop transaminase elevations which meet our study criteria for the diagnosis of viral hepatitis. This may indicate either transmission of non-A, non-B hepatitis by routes other than blood, or that there is a low level of transient transaminase elevation in the general population which is not of viral etiology, (nor is it due to alcoholism, drug toxicity, or congestive heart failure). When analysis is completed, the prospective study will also answer several peripheral issues relating to the occurrence of PTH. These include the significance of an elevated transaminase level in the donor, the significance of antibodies to the hepatitis B surface and core antigens in the donor, and the role of transfusion volume.

The finding that most PTH is due to non-A, non-B agent(s) has stimulated additional investigations to study the clinical course of non-A, non-B, particularly its role in chronic hepatitis, to determine the number of infectious agents involved, and to develop a test system for detecting these agents. Clinically the most important feature of non-A, non-B is that it presents as anicteric disease in 75% of cases and progresses to chronic disease in almost 50% of cases. The chronic disease is primarily chronic active hepatitis (CAH), as determined by liver biopsy; but long term follow-up suggests that this CAH is more benign than that associated with drug toxicity or autoimmune phenomena. The trend appears to be for a very slow resolution of biochemical abnormalities and, in one case, when rebiopsied, for histologic improvement. In collaboration with the Liver Unit of NIAMDD, we have initiated a long-term follow-up of such cases including annual liver biopsy where indicated. It is hoped that this will better elucidate the natural history of a very prevalent form of chronic liver disease.

One of the most significant research developments this year stems from collaborative work with the Laboratory of Infectious Diseases, NIAID. Last year we demonstrated transmission of non-A, non-B viral hepatitis to the chimpanzee. This year, using infectious inocula from our heart surgery patients, Dr. Shimizu of NIAID has examined the liver tissue of chimpanzees with hepatitis by thin-section electron microscopy and has described two distinct morphologic changes: 20-27 nm intranuclear particles (strain H) and double-unit membraned, tubular, cytoplasmic inclusions (strain F), the latter seemingly contiguous with the rough endoplasmic reticulum. These changes were not seen in animals with other forms of viral hepatitis nor in liver biopsies prior to the onset of non-A, non-B hepatitis. Most significanctly, each chimp had one or the other of these changes, but never both. Although these changes do not appear to represent viral particles per se, the specificity of these EM findings and the clear separation into two morphologic types provide the most concrete evidence to date that there is more than one non-A, non-B agent. We have also approached this question by cross challenge studies in five chimps initially infected by five separate patient inocula. None of these chimps developed a second bout of hepatitis when cross-challenged. However, it now appears that all chimps were challenged with strain F material, hence homologous immunity would have been expected. We are now challenging previously infected strain F animals with a strain H inoculum. If they become infected, this will provide further evidence for at least two immunologically distinct non-A, non-B agents.

Studies to develop tests for non-A, non-B hepatitis have thus far been unsuccessful. Using new reagents, we are typing to develop a solid phase radioimmunoassay. We will also try to confirm a promising counterelectrophoresis method described by researchers at the Bureau of Biologics. We continue to also work with Dr. Jules Dienstag of Harvard Medical School to see if we can disassociate a non-A, non-B antigen or antibody from immune complexes. Our preliminary study this year showed (by the RAJI cell assay) that immune complexes are present in the sera of patients with non-A, non-B hepatitis. The specificity of these complexes for non-A, non-B has, however, not yet been established.

Another major area of involvement for the BBD has been in the clinical evaluation of a hepatitis B vaccine. In a collaborative study with the New York Blood Center, we are now completing a baseline surveillance study in the major dialysis centers of the Washington area. In September, we will begin hepatitis B vaccine efficacy trials among the patients and staffs of these centers. An effective vaccine could have a major impact on the management of this high risk population.

A cooperative study engendered by a Soviet-American health exchange agreement was undertaken to compare the frequency of hepatitis virus antigens and antibodies among blood donors in the USSR and the USA. Age and sex stratified blood donors were sampled from different geographic areas. Serums were divided in half for testing in both countries for hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBs), antibody to hepatitis B core antigen (anti-HBc), and antibody to the hepatitis A virus (anti-HAV).

A total of 994 Soviet donor serums from five different regions and 1178 American donor serum from six different regions were evaluated in both countries and the results compared. Among the Soviet donors there were 38 (3.8%) HBsAg-positive donors; among the American donors, there were six (0.5%) with HBsAg. Donors with only anti-HBc (no HBsAg or anti-HBs detectable) numbered 76 (7.6%) among those from the USSR and eight (0.7%) from the USA. Among the Soviet donors, 450 (45%) had some markers of exposure to the hepatitis B virus; while among the American donors, 94 (8%) did. For anti-HAV 848 (85%) of the Soviet donors were positive, compared to 403 (34%) of the American donors.

The serum testing resulted in new information on the prevalence of markers of viral hepatitis among both Soviet and American donors. No comparable information on healthy blood donors from varied geographic areas in each country was available previously. The results permit calculation of age and sex prevalence of hepatitis B and hepatitis A markers within each country and between the two countries and allow comparison of methodologies in use in the Soviet Union and the United States.

## Immunohematology

Our Immunohematology Laboratory continues its investigations into the nature of red cell antigens and antibodies. In collaboration with the Microbiology Section of Clinical Pathology, we have demonstrated the acquisition of some usually genetically determined red cell antigens during bacterial sepsis. It now appears that several bacterial organisms have the ability to confer Jk-like antigen onto red cells and to induce anti-Jk in patients. Conversely, this laboratory has demonstrated loss of inherited red cell antigens of the ABO, I and Lewis systems in patients with various forms of malignancies. Studies are also being carried out in collaboration with NCI to measure soluble blood group substances in breast cyst fluids of malignant as opposed to benign tumors.

As a follow-up to our joint finding that Duffy blood group antigens play a key role in the invasion of human red cells by the P. vivax malaria parasite, studies are continuing with Dr. Louis Miller of NIAID to biochemically analyze the Duffy determinants which serve as P. vivax receptors. Additional studies are aimed at establishing a receptor for P. falciparum. Preliminary evidence indicates it may be in the MNS system of red cell antigens. Lastly, work is being conducted with Dr. Victor Ginsberg of NAIMDD on the biochemistry of soluble blood group substances.

## Clinical Immunohematology

This Department continues its efforts to determine the in-vivo significance of red cell antibodies. Many patients have been studied by $^{51}$Cr red cell survival; it has become evident that a 24 hour post-transfusion survival is more indicative of the safety of transfused blood than the previously recommended one hour survival. Using this technique, two patients have been studied and reported who had accelerated immune destruction of transfused cells without detectable antibody. In another study, the survival characteristics of Lewis-positive cells in recipients with anti-Lewis antibody are being investigated; it is not clear at present how often such antibodies have clinical significance.

As part of a partial red cell exchange protocol, we have studied patients with sickle cell anemia who experienced delayed hemolytic transfusion reactions simulating sickle cell crises. Each apparent crisis coincided with the disappearance of transfused cells and the appearance of irregular alloantibodies.

As part of an ongoing study, 76 donors with a history of recent or severe penicillin allergy have been screened with hemagglutinating and RAST tests for penicillin antibody. Blood units from these donors have been followed to see if an allergic reaction might occur in recipients who are receiving penicillin. The results thus far are inconclusive.

Pheresis and Component Therapy

The Blood Bank is actively engaged in studies which utilize new technology in automated pheresis and cell separation. In collaboration with NHLBI, NCI and Clinical Pathology's Hematology Section, separation of young red cells or "neocytes" from the blood of normal donors is being carried out. Such red cells, with an average age of 25-30 days, can decrease by half the transfusion requirement of chronically transfused patients and thus considerably decrease the risk of iron overload, currently a critical factor in their life expectancy. To date $^{51}$Cr survival studies have been performed in four thalassemic patients receiving neocytes and one thalassemic is being totally supported on such transfusions.

In cooperation with the Clinical Hematology Branch of NHLBI, the study of automated exchange transfusion in sickle cell anemia continues. Evaluation of exercise tolerance and oxygen saturation before and after exchange are an integral part of this protocol.

Plasma exchange for systemic lupus erythematosis is being evaluated in a controlled, blinded study performed with investigators of NIAMDD. An additional, controlled study with NHLBI is evaluating plasma exchange in pure red cell aplasia and aplastic anemia.

A form of chronic lung disease is associated with a deficiency of a trace protein in plasma, alpha 1-antitrypsin. This protein is being prepared from stored plasma and then transfused to deficient patients. One such preparation has been shown to have a normal half life and to appear in the lung as hoped. Long term observation will be required to see if such replacement therapy will reduce the frequency of chronic lung disease in patients who lack alpha-1-antitrypsin.

## IV. Future Objectives

In Section I the missions and goals of this Department were outlined. In order that these goals may be achieved, specific objectives have been established. It is through the timely meeting of these objectives that our three primary missions - service, teaching, and research will be accomplished.

Service: We wish to increase our capacity and expertise in component preparation and therapy. Future objectives are to expand the newly established Hemotherapy Center so that it will be the primary therapeutic and support pheresis unit for the Clincial Center. It is planned that this unit will eventually be staffed and operational from 8 a.m. to 9 p.m. daily, and that full use will be made of the IBM 2997 and Haemonetics Model 30 Automated Blood Cell Processors. This Center will be housed temporarily in a trailer adjacent to the Blood Bank but will eventually move to permanent quarters in space currently occupied by the CC South Clinic. The Hemotherapy Center will eventually assume full responsibility for the plateletpheresis operation currently managed by an NCI contract. Provision of this service by the Blood Bank is a logical and economical move and will be provided when additional space becomes available to the Blood Bank, (upon completion of the ACRF) and slots for staff are secured.

Objectives related to the service goal of increasing our donor base include expanding recruiting efforts and blood drives at off-campus buildings such as Westwood and Landow. Innovative methods for recruiting more on-campus donors, such as recognition of multi-unit donors and increased use of displays and publications, are planned. Under study is a proposal to establish a satellite blood donor station in the Occupational Health Unit in Building 31.

Teaching: The medical technology school affiliation will expand to include students from Columbia Union College as well as Montgomery Community College. The training program for Specialists in Blood Banking (SBB) will increase from three to four students, and the curriculum will be further revised and updated. The Clinical Pathology residents' training rotation will be modified to include revised and expanded sections in automated pheresis, HLA typing, and hemolytic disease of the newborn. The Blood Bank physician-fellow will be provided more structured research guidance. A further teaching objective is to review, and possibly revise the FAES course, Immunohematology and Blood Banking, Immunology 508M.

Research: Objectives in hepatitis research include expanded investigation into the pathophysiology and modes of transmission of non-A, non-B hepatitis virus or viruses. Ongoing evaluation of post-transfusion hepatitis through careful follow-up of cardiac surgery patients will continue. Our objectives in immunohematology research include an investigation, in depth, of the relationship between red cell antigenic changes and certain disease states, the characterization of unusual red cell antibodies through 51 chromium red cell survival studies, and the conclusion of an investigation of the relationship between penicillin allergy and transfusion reactions. The new Hemotherapy and HLA units will increase our study of the usefulness of young red cells ("neocytes") in the chronically transfused patient, continue investigation of the effect of plasma exchange, e.g., in patients with systemic lupus erythematosis, and explore investigating the relationship of HLA antibodies to febrile non-hemolytic transfusion reactions.

The Blood Bank Staff looks forward to the successful attainment of these objectives and goals. Our Department continues to fulfill its mission of better patient care through service, teaching, and research activities.

# BLOOD BANK DEPARTENT ORGANIZATIONAL CHART

## BLOOD SERVICES SECTION

### Laboratory Section

Casper
Codell
Coles
Dorset
Eberhard
Ellis
Gregg
Gundry
Kolasinski
Sigmon
Simpkins

Gustafson
(Supervisor)

Rosen

### Nursing Unit

Chance
Davis
Leach
Mason

Yanchulis
(Supervisor)

Ennis
Kent
Meyers
Moroney
Nilsen
Weber
Wells

Chappell
(Supervisor)

CHIEF: KLEIN

## IMMUNOLOGY SECTION

### Hepatitis

James
Shoup

Koziol
(Supervisor)

Solomon

### Immunohematology

McGinniss

Davey

CHIEF: ALTER

## OFFICE OF THE CHIEF

Chichester
Kilmain
Orr
Shawver

### Recruiting

Brown
Driscoll
Kendall
Rosenberg

Colbert
(Supervisor)

CHIEF: HOLLAND

## PUBLICATIONS

1. Alter, H. J., Purcell, R.H., Feinstone, S.N., Holland, P.V., and Morrow, A.G.: Non-A, non-B Hepatitis. A Review and Interim Report of an Ongoing Prospective Study. Proc. of the Second USCF Symposium on Viral Hepatitis. In Vyas, G.N., Cohen, S.N., and Schmid, R. (Eds.): Viral Hepatitis. Philadelphia, Franklin Institute Press, 1978, pp. 359-369.

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11. Holland, P.V.: Discussion of paper by Dr. M.Goldfield entitled, "Control of Posttranfusion Hepatitis." Proc. of the Second UCSF Symposium on Viral Hepatitis. In Vyas, G.N., Cohen, S.N, and Schmid, N. (Eds.): Viral Hepatitis. Philadelphia, Franklin Institute Press, 1978, pp. 415-417.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-02001-04 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
$^{51}$Cr RBC Survival as a Means of Defining the in vivo Characteristics of Red Cell Alloantibodies

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Richard Davey, M.D., Senior Investigator, Blood Bank Department, CC

Other: Paul V. Holland, M.D., Chief, Blood Bank Department, CC
Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank, CC
Sandra L. Rosen, M.T. (ASCP)

COOPERATING UNITS (if any)

LAB/BRANCH
Blood Bank Department

SECTION
Immunology

INSTITUTE AND LOCATION
Clinical Center, Building 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
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CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER
☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

In the first phase of this project the rapid sequence $^{51}$chromium red cell survival test proved to be a valuable test in the evaluation of the clinical significance of irregular red cell antibodies. It is now a widely accepted laboratory procedure used primarily in situations when compatible blood cannot be found by usual in vitro serologic techniques.

The project, therefore, now concentrates on those patients and blood donors who have poorly understood and incompletely characterized red cell antibodies detected in their serum. Characterization of the in vivo significance of these antibodies will allow more rational selection of blood for these people should transfusion be necessary in the future.

A study of the significance of anti-H in the rare "Bombay" patient has recently been published, and two papers describing unusual serologic problems solved by the $^{51}$Cr technique are in press. Studies continue investigating the significance of the Lewis antibody and, in collaboration with the Red Cross, the clinical significance of certain variations observed in the direct antiglobulin test.

PHS-6040
(Rev. 10-76)

Z01-CL-02001-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: A Rapid Technique for Determining In-Vivo Red Cell Survival in Patients Demonstrating In-Vitro Incompatibility with all Donor Red Cells

Previous Serial Number: Z01-CL-02001-03 BB

Principal Investigator: Richard J. Davey, M. D.

Other: Paul V. Holland, M. D.
Harvey J. Alter, M. D.
Sandra L. Rosen, M. T. (ASCP)

Cooperating Units: None

Man Years: Total: 1
Professional: 1

## Project Description

### Objective:

1. To utilize a rapid $^{51}$Cr survival procedure to clarify the clinical significance of certain poorly understood or incompletely characterized red cell antibodies (e. g. anti-H in Bombay O, anti-Chido).

### Methods Employed:

A small sample (1.0 - 2.0 ml) of test red cell suspension is labeled with 20 u Ci of $^{51}$Cr, washed, and infused into the patient. Serial blood samples are subsequently drawn and the survival characteristics of the infused cells determined by measuring the radioactivity of each sample.

### Major Findings:

Since approval of this study the following observations have been made.

A. Two unusual cases of "saline agglutinating phenomenon" have been documented and described. Patients with this phenomenon have a serum factor which agglutinates all red cells which have been washed in saline, thus complicating laboratory crossmatching efforts and rendering the infusion of saline containing fluids potentially hazardous. Survival studies using cells washed in various media permitted a decision to be made which resulted in a safe open-heart surgical procedure being done on one patient.

B. People with the rare inherited blood group called "Bombay O" have in their serum an antibody which reacts in-vitro against all normal ABO blood groups. The clinical significance of this antibody was investigated through $^{51}$Cr survival studies in a person with the "Bombay O" blood group. It was determined that the antibody was strongly active in-vivo and that "Bombay O" people can safely receive blood only from other "Bombay O" donors.

C. Patients who required transfusion with panagglutinating antibodies and with antibodies against high incidence or poorly described RBC antigens were studied. The clinical significance of each patient's antibodies was determined by a $^{51}$Cr survival study, with decisions made as to the relative safety of transfusion.

D. A series of patients with the commonly encountered alloantibody, anti-Lewis , are being studied. The in-vivo potency of this antibody has never been clearly defined. If it proves to be of little in-vivo significance, transfusion of patients with the antibody will be considerably easier.

E. Two patients with delayed hemolytic transfusion reactions but without serologic evidence of incompatibility were found to have shortened $^{51}$Cr rbc survival of the implicated units.

## Significance to Biomedical Research and the Program of the Institute

The primary goal of the Clinical Center Blood Bank is to provide safe blood products to Clinical Center patients. This $^{51}$Cr red cell survival procedure has proven to be a valuable tool in defining the relative safety of transfusion in patients for whom compatible blood cannot be found by in-vitro techniques. If this procedure continues to prove its significant clinical value, it is hoped that it will become a widely used blood bank service. In addition, use of this technique will provide greater understanding of the clinical importance of certain red cell antibodies which are now incompletely characterized.

## Proposed Course:

Continued use of $^{51}$Cr survival technique in appropriate patients.

## Publications:

1. Davey, R., Tourault, M., and Holland, P.: Significance of Anti-H in the Bombay (O$_h$) Patient, Transfusion 18: 738, 1978.

2. Davey, R., Gustafson, M., and Holland, P.: Accelerated Immune Red Cell Destruction in the Absence of Serologically Detectable Alloantibodies, Transfusion. In Press.

3. Davey, R., O'Gara, C., and McGinniss, M.: Incompatibility In Vitro and In Vivo Demonstrated Only With Saline Suspended Red Cells. Vox Sang. In Press.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-02002-04 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Use of Hepatitis B Immune Globulin Following Accidental Exposure to HBV

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey G. Klein, M.D., Chief, Blood Services Section, Blood Bank Department, CC

Other: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank, CC
Paul V. Holland, M.D., Chief, Blood Bank, CC
David DeMets, Ph.D., Biometrics Researcher, National Heart, Lung, and Blood Institute

COOPERATING UNITS (if any)
NHLBI

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

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☐ (a1) MINORS ☒ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Two recently reported, randomized, double blinded trials have demonstrated the efficacy of high titer hepatitis B immune globulin (HBIG) in affording temporary passive immunity to individuals accidentally exposed to low doses of HBsAg-positive material. In both studies, a 5 ml injection of HBIG was given within one week of exposure and a second injection one month later. This dosage schedule was chosen arbitrarily.

A single dose schedule of HBIG has proven efficacious in prophylaxis of spouses exposed to hepatitis B. However, these two dosage schedules, single injection and divided injections, have never been compared in a controlled study. This study plans to enroll 300 individuals accidentally exposed to hepatitis B positive materials for development of hepatitis. Candidates were to be randomized in a double blinded fashion and treated with the same dose of HBIG in either a single or double injection. Two hundred and ninety-six individuals have been enrolled. Samples were collected at monthly intervals, following exposure, for six months and at 9 and 12 months.

PHS-6040
(Rev. 10-76)

Z01-CL-02002-04-BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Comparison of single dose and divided dose administration schedules of Hepatitis B immune globulin: Efficacy in preventing hepatitis B following accidental exposure (needle stick).

Previous Serial Number: Z01-CL-02002-03-BB

Principal Investigator: Harvey G. Klein, M.D.

Other: Harvey J. Alter, M.D.
Paul V. Holland, M.D.
David DeMets, Ph.D.

Cooperating Units: NHLBI

Man Years: Total: 2
Professional: 1
Other: 1

## Project Description

### Objectives:

To determine whether a single injection of hepatitis B immune globulin (HBIG) is as effective as a divided dose injection schedule in preventing hepatitis B caused by accidental exposure.

### Methods Employed:

Exposed individuals are referred by telephone to the Clinical Center Blood Bank. The purpose of the study is explained, and a telephone questionnaire is used to determine eligibility for study.

Individuals who qualify are required to send blood specimens to the Blood Bank to assure exposure to an infectious source and susceptibility of the individual. Simultaneously, the individual is supplied with an informed consent form which further explains the purpose of the study.

Individuals who enter the study are randomized in a double blinded fashion to the single injection or divided dose schedule. Each receives the same total dose of HBIG. Serial blood samples are mailed and a follow-up clinical symptom questionnaire must be completed at month 6 and month 12.

### Major Findings:

Two hundred and ninety-six individuals have been entered, and 171 have completed the 12 month followup. The two injection regimen patient group experienced less hepatitis than the single injection group. We are in the final stages of the follow-up period. HBsAg-positive "donor" samples have been tested for HBeAg and anti-HBe to see how these markers correlate with their infectivity.

### Significance to Biomedical Research and Programs of the Institute

The Clinical Center Blood Bank has had a longstanding interest in the problem of hepatitis caused by blood and blood products. This study should (1) add further information about the natural history of hepatitis following HBIG administration (2) answer the question of whether a single injection is as effective as a divided dose schedule, a question of great practical importance and (3) provide valuable serum samples for studying other markers of hepatitis and hepatitis infectivity.

### Proposed Course:

The study has been completed, but statistical evaluation has not been finished.

### Publications:

1. Klein, H.G., Alter, H.J. and Holland P.V.: Postexposure Immunoglobulin Prophylaxis of Hepatitis B; a Comparison of Two Dosage Schedules. Proc. of the Second UCSF Symposium on Viral Hepatitis. In Vyas, G. N., Cohen, S. N., and Schmid, N. (Eds.): *Viral Hepatitis*. Philadelphia, Franklin Institute Press, 1978, pp. 483-486.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01-CC-02003-05 BB

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
"Role of Hemagglutinating and IgE Penicillin Antibody in Donor Blood"

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigators: Richard J. Davey, M.D.
Senior Investigator Clinical Center Blood Bank
Mary H. McGinniss, AB(ASCP)SBB
Research Biologist Clinical Center Blood Bank

Other: Harvey J. Alter, M.D., Chief, Immunology Section
Clinical Center Blood Bank

COOPERATING UNITS (if any)

LAB/BRANCH
Blood Bank Department

SECTION
Immunology

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10A, Room 1E33, NIH, Bethesda, Md. 20205

TOTAL MANYEARS: 0.5
PROFESSIONAL: 0.5
OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Several years ago it was reported by us that some patients on penicillin therapy, when transfused with donor blood containing hemagglutinating penicillin antibody, suffered an untoward reaction similar to anaphylaxis or serum sickness. We are attempting to establish a prospective, control study to determine if passively transferred anti-penicillin antibody can induce allergic manifestations in patients who are receiving penicillin or penicillin derivatives as part of their therapy. Donors will be screened for a history of penicillin hypersensitivity and their blood will be tested for anti-penicillin antibodies by hemagglutination and radioimmunoassay techniques. Recipients of blood from donors with a history of penicillin hypersensitivity will be followed for untoward reactions following penicillin therapy and will also be tested for IgG and IgE anti-penicillin antibodies. Appropriate controls will be similarly followed.

Serial No. Z01-CC-02003-05 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Passive Transfer of Penicillin Hypersensitivity in Transfused Blood

Previous Serial Number: Z01-CC-02003-04 BB

Principal Investigators: Richard J. Davey, M.D.
Mary H. McGinniss, AB(ASCP)SBB

Other Investigators: Harvey J. Alter, M.D.

Cooperating Units: Inside NIH
None

Outside NIH
None

Many Years: Total: 0.5
Professional: 0.5
Other: 0

## Project Description

### Objectives:

A. To study the incidence and type of untoward reaction patients on penicillin therapy may experience when tranfused with blood from a donor having a history of penicillin allergy and/or hemagglutinating or IgE penicillin antibody.

B. To gather data on the number of NIH donors having these types of antibodies and to do a statistical analysis on the data.

### Methods Employed:

1. All donors will be questioned regarding a history of penicillin allergy. Those with such history will be divided into those with anaphylactic reactions and those with just rash. The next consecutive donor after the donor giving a positive history of penicillin allergy will serve as a control.

2. An aliquot of serum will be obtained from both allergic and control patients and the aliquot tested for IgM, IgG (hemagglutination) and IgE (RAST) anti-penicillin antibody.

3. Recipients of blood from allergic and control patients will be followed for untoward reactions occurring within 48 hours of transfusion. Such reactions will be correlated with whether or not the recipient is being treated with penicillin or a penicillin derivative.

4. Pre and post transfusion samples will be obtained from those recipients who received blood from a donor with detectable anti-penicillin antibody to determine if passive transfer can be documented.

Major Findings:

In 1971, at the American Association of Blood Banks meeting, we reported findings in three patients on penicillin suffering untoward reactions which retrospectively could only be attributed to the passive infusion of penicillin antibody in donor blood. This was the impetus for the present study.

In the original study, of 29 patients who received a unit(s) of blood known to contain hemagglutinating penicillin antibody, three (10%) had untoward reactions of the serum sickness variety which could not be attributed to any other factor.

Subsequently 9 new cases of possible urticarial or serum sickness type of reactions following blood transfusion to patients receiving penicillin have been observed. A causal relation between donor anti-penicillin antibody and recipient reaction has, however, been difficult to document because the radioimmunoassay for IgE anti-penicillin antibodies is not working optimally.

Significance to Biomedical Research and the Program of the Institute:

A. Identification of another possible cause of untoward reaction of blood transfusion.

B. If it can be shown that some penicillin reactions in patients are due to passive transfer of anti-penicillin antibody, then such patients will not need to be restricted from future penicillin therapy.

C. Similary if it can be shown that such a mechanism for penicillin reactions exists, then patients being treated with penicillin will have to receive blood from donors without a history of penicillin allergy and/or without demonstratable anti-penicillin antibodies.

Proposed Course:

Setting up a working radioimmunoassay test for detecting IgE penicillin antibody, continued testing of new NIH donors for hemagglutinating penicillin antibody and monitoring of patient's response to such transfusions.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02005-10 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Prospective Study of Post-transfusion Hepatitis in Open Heart Surgery Patients

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, Clinical Center Blood Bank

Other: Paul V. Holland, M.D., Chief, Clinical Center Blood Bank
Robert H. Purcell, M.D., Head, Hepatitis Virus Section, LID, NIAID

COOPERATING UNITS (if any)
NIAID, NHLBI

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>12 | PROFESSIONAL:<br>4 | OTHER:<br>8 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☒ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

To prospectively follow all adult patients undergoing open heart surgery for the development of post-transfusion hepatitis and by appropriate serologic tests to determine the causative agents. Primarily interested in investigating the incidence of "non-A, non-B" hepatitis and to see if there are any epidemiologic or serologic clues to its prevention. This study will also compare the clinical course of the various forms of PTH and determine the frequency with which chronic hepatitis develops.

Serial No. Z01-CL-02005-10 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Prospective Study of Posttransfusion Hepatitis (PTH) in Open Heart Surgery Patients

Previous Serial Number: Z01-CL-02005-09 BB

Principal Investigator: Harvey J. Alter, M.D.

Other Investigators: Robert Purcell, M.D.
Paul V. Holland, M.D.

Cooperating Units: Inside NIH
NIAID, NHLBI

Outside NIH
None

Man Years: Total: 12
Professional: 4
Other: 8

## Project Description

### Objectives:

1. To prospectively follow all adult patients undergoing open heart surgery at NIH for evidences of PTH.

2. To determine the relative occurrences of type B, type A and type non-A, non-B hepatitis.

3. To determine the effectiveness of various tests for HBsAg for screening blood donors.

4. To compare the clinical course of the various forms of PTH and to determine the frequency with which chronic hepatitis develops.

5. To develop improved screening methods for type B and type non-B hepatitis.

Methods:

1. All adult patients undergoing open heart surgery are followed for six to nine months with serial tests for SGPT, HBsAg and anti-HBs.

2. Cases of hepatitis are additionally tested for serologic response to CMV, EBV and the hepatitis A virus; if type B disease, they are tested for anti-core antibody, e antigen, DNA polymerase and are subtyped.

3. Donors are tested by the most sensitive methods for HBsAg currently available. In addition donors will be tested for SGPT to see if this relates to recipient hepatitis.

Major findings: Studies to date have demonstrated:

1. The increased risk of blood containing HBsAg.

2. A 90% reduction in hepatitis by exclusion of commercial and HBsAg positive donors.

3. The superiority of RIA over CEP as a donor screening method.

4. The fact that approximately 90% of PTH is now due to a previously unrecognized virus (or viruses) currently termed "non-A, non-B."

5. That the type A hepatitis virus is almost never implicated in PTH: neither have the CMV or EBV been implicated in our cases.

6. That non-A, non-B hepatitis is generally less acutely severe than type-B but that it tends to frequently become chronic.

Significance to Biomedical Research and the program of the Clinical Center:

These studies have been instrumental in establishing many key points concerning the frequency, etiology and prevention of PTH at the Clinical Center and across the United States.

Proposed Course: See objectives and methods.

Publications:

Holland, P.V., Alter, H.J., Purcell, R.H., Walsh, J.H., Morrow, A.G., and Schmidt, P.J.: The Infectivity of Blood Containing the Australia antigen. In Prier, J.E. and Friedman, H. (Eds.): Australia Antigen. Baltimore, University Park Press, 1973, pp. 205-211.

Alter, H.J., Holland, P.V., Purcell, R.H., Lander, J.J., Feinstone, S.M., Morrow, A.G., and Schmidt, P.J.: Posttransfusion Hepatitis after Exclusion of the Commercial and Hepatitis B Antigen Positive Donor. Ann. Int. Med. 77: 691-699, 1972.

Feinstone, S. M., Kapikian, A. Z., Purcell, R. H., Alter, H. J., and Holland, P. V.: Transfusion-associated Hepatitis Not Due to Viral Hepatitis Type A or B. *N. Eng. J. Med.* 292: 767-770, 1975.

Alter, H. J., Holland, P. V., and Purcell, R. H.: The Emerging Pattern of Post-transfusion Hepatitis. *Am. J. Med. Sci.* 270: 329-334, 1975.

Alter, H. J., Purcell, R. H., Holland, P. V., Feinstone, S. M., Morrow, A. G., Moritsugu, Y.: Clinical and Serological Analysis of Transfusion-Associated Hepatitis. *Lancet* 2: 838-481, 1975.

Alter, H. J., Purcell, R. H., Feinstone, S. N., Holland, P. V., Morrow, A. G.: Non-A, Non-B Hepatitis: A Review and Interim Report of an Ongoing Prospective Study. Proc. of the Second UCF Symposium on Viral Hepatitis In Vyas, G. N., Cohen, S. N. and Schmid, R. (Eds.): *Viral Hepatitis*, Philadelphia, Franklin Institute Press, 1978, pp. 359-369.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-02010-05 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Chronic Sequelae of Non-A, Non-B Hepatitis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Jay Hoofnagle, M. D., Senior Investigator, NIAMDD

Other: Harvey J. Alter, M. D., Chief, Immunology Section, Blood Bank, CC
Robert Purcell, M. D., Head Hepatitis Virus Section, LID, NIAID
Anthony Jones, M. D., Chief, Section on Diseases of the Liver, DDB, NIAMDD
Kamal Ishak, M. D., Armed Forces Institute of Pathology

COOPERATING UNITS (if any)
NIAID, NIAMDD

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>2 | PROFESSIONAL:<br>2 | OTHER: |

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER
☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

All patients developing non-A, non-B hepatitis following open heart surgery will be followed with serial studies of SGPT to determine the incidence of chronic liver disease and to compare this incidence with those having type B hepatitis. Liver biopsy will be obtained when the SGPT is elevated for more than 6 months and then again at one and three years. Biopsy material will be obtained for fluorescent and EM studies, as well as light microscopy with multiple stains.

PHS-6040
(Rev. 10-76)

Serial No. Z01-CL-02010-05 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Chronic Sequelae of Non-A, Non-B Hepatitis

Previous Serial Number: Z01-CL-02010-04 BB

Principal Investigator: Jay Hoofnagle, M.D.

Other: H. Alter, M.D.
R. Purcell, M.D.
A. Jones, M.D.
K. Ishak, M.D.

Cooperating Units: Inside NIH
NIAID, NIAMDD

Outside NIH
Armed Forces Institute of Pathology

Man Years: Total: 2
Professional: 2

## Project Description

Objectives:

1. To establish long-term follow-up of patients identified as having non-A, non-B hepatitis in post-transfusion hepatitis (PTH) studies conducted at NIH since 1970.

2. To determine by SGPT the frequency of chronic hepatitis.

3. To determine by liver biopsy the histologic pattern of non-A, non-B hepatitis and to save biopsy specimens for immunofluorescent and EM studies.

4. To follow the natural history of chronic non-A, non-B hepatitis.

Methods Employed: See objectives

Major Findings:

Chronic hepatitis frequently follows acute non-A, non-B hepatitis. In the patients thus far biopsied the histologic picture is similar to chronic type B hepatitis, showing features of either chronic persistent or chronic active hepatitis.

Significance to Biomedical Research and the Program of the Clinical Center:

Non-A, non-B hepatitis now accounts for 80% to 90% of PTH and is thus a major transfusion hazard. While it tends to be less acutely severe than type B hepatitis, preliminary evidence suggests that it progresses to chronic hepatitis with considerable frequency. Very little is known about this disease and it is imperative that clinical and serologic studies be undertaken. It is possible that a high percentage of chronic active hepatitis and cryptogenic cirrhosis represent the chronic sequelae of a previously unrecognized case of anicteric non-A, non-B hepatitis.

Proposed Course: See objectives

Publications:

1. Berman, M., Alter, H. J., Ishak, K.G., Purcell, R.H., and Jones, E.A.: The Chronic Sequelae of Non-A/Non-B Hepatitis. Annals of Int. Med. 91: 1-6, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02011-05-BB |

PERIOD COVERED

October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

The Duffy Blood Group Determinant and Susceptibility to Malaria

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Louis H. Miller, M.D., Head Malaria Section, LPD, NIAID

Other: Mary McGinniss, AB(ASCP)SBB, Research Biologist, Clinical Center Blood Bank
Paul V. Holland, M.D., Chief, Clinical Center Blood Bank

COOPERATING UNITS (if any)

Laboratory Parasitic Diseases, NIAID

LAB/BRANCH

Blood Bank Department

SECTION

Immunology Section

INSTITUTE AND LOCATION

Clinical Center, Bldg. 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 2 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☑ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Working with an in vitro model for invasion of red cells by malaria merozoites, this study has demonstrated that human red cells lacking the Duffy a and b antigens are resistant to invasion. This corresponds well with epidemiologic studies which show that approximately 70% of West African and American blacks are resistant to Vivax malaria. A similar proportion of these blacks are Duffy a and b negative whereas the Duffy negative genotype is extremely rare in other racial groups. The close association between the Duffy negative genotype and resistance to Vivax malaria has also been confirmed by retrospective analysis of 11 volunteers experimentally inoculated with P. vivax. A retrospective study of U.S. servicemen who contracted malaria in South East Asia has been completed and confirmed again our original hypothesis. A second study conducted by CDC in Honduras has also been completed and is another in-vivo study in-proof.

Serial No. Z01-CL-02011-05-BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: The Duffy Blood Group Determinant and Susceptibility to Malaria

Previous Serial Number: Z01-CL-02011-04-BB

Principal Investigator: Louis H. Miller, M.D.

Other: Mary H. McGinniss, AB(ASCP)SBB
Paul V. Holland, M.D.

Cooperating Units: Lab. Parasitic Disease, NIAID

Man Years: Total: 2
Professional: 2

## Project Description

### Objectives:

A. To use a red cell culture technique to determine if invasion of erythrocytes by *Plasmodium falciparum* is dependent upon antigenic determinants on the erythrocyte membrane similar to that found for *Vivax* malaria.

B. To characterize the antigens involved and determine the sequence of events when malarial invasion occurs.

C. To determine if RBC antigens are involved in other, less known forms of malaria and other parasitic diseases using the RBC as part of its life cycle.

### Methods Employed:

1. *P. falciparum* merozoites are added to RBC in culture and the degree of RBC invasion is observed microscopically. The degree of invasion of RBC with differing phenotypes is compared.

2. When a specific antigen is identified as being involved in the attachment or invasion by malaria parasites (as in (1)), attempts are made to block or destroy that site with specific antibody or enzyme treatment.

3. Blood samples from donors of rare MNS system phenotypes are being collected to test with *P. falciparum* parasites.

## Major Findings:

Last year, one cell among many tested was not invaded normally by P. falciparum parasites. This was a very rare cell known as En(a-). Repeat testing did not enhance our feeling that this cell might hold the clue to a red cell invasion receptor. Instead, we have shifted to testing various trypsin treated cells because this treatment, of itself, reduces invasion of cells by 50-75%. One cell, when trypsin treated, a S neg s neg U neg cell, showed 95% reduction of invasion; therefore, we suspect that S or s antigens might be involved. Work is continuing using rare red cells which genetically lack these antigens or do not express these antigens adequately.

A new finding concerning P. vivax is that anti-$Fy^3$ , in addition to anti-$Fy^a$ and Fy $^b$, when added to $Fy^a$ or $Fy^b$ positive cells, will block invasion of P. vivax merozoites. This confirms our latest hypothesis that the invasion receptor is not $Fy^a$ or $Fy^b$, per se, but rather is an, as yet, unidentified part of the Duffy molecule.

## Significance to Biomedical Research and the Program of the Institute:

A. Elucidation of the mechanisms of red cell invasion by P. falciparum.

B. Increased knowledge of erythrocyte polymorphisms.

C. Accumulation of data which could culminate in a vaccine or other immunologic means of malaria prevention.

## Publications

1. Miller, L.H., Mason, S.J., Dvorak, J.A., McGinniss, M.H., and Rothman, I.K.: Erythrocyte Receptors for Plasmodium knowlesi Malaria: The Duffy Blood Group Determinants. Science. 159: 561-563, 1975
2. Miller, L.H., Mason, S.J., Clyde, D.F., and McGinniss, M.H.: The Resistance Factor to Plasmodium vivax in Blacks. N. Eng. J. Med. 295: 302-304, 1976.
3. Miller, L.H., Haynes, J.D., McAuliffe, F.M., Shiroishi, T., Durocher, J.R., and McGinniss, M.H.: Evidence for Differences in Erythrocyte Surface Receptors for the Malarial Parasites, Plasmodium falciparum and Plasmodium knowlesi. J. Exp. Med. 146: 277-281, 1977.
4. Mason, S.J., Miller, L.H., Shiroishi, T., Dvorak, J.A., and McGinniss, M.H.: The Duffy Blood Group System and Susceptibility to Plasmodium knowlesi Malaria. Brit. J. Haem. 36: 327-335, 1977.
5. Miller, L.H., McGinniss, M.H., Holland, P.V., and Sigmon, P.: The Duffy-Group Phenotype in American Blacks Infected with Plasmodium vivax in Vietnam. Am. J. of Trop. Med. and Hyg. 27: 1069-1072, 1978.

6. Spencer, H.C., Miller, L.H., Collins, W.E., Knud-Hansen, C., McGinniss, M.H., Shiroishi, T., Labos, R.A., and Feldman, R.A. The Duffy Blood Group and Resistance to *Plasmodium vivax* in Honduras. *Am. J. Trop. Med. and Hygiene*. 27: 664-670, 1978.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02012-03 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Chido (Ch$^a$) Antibody Production Induced by Cancer Immunotherapy

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Mary L. Gustafson, MS, MT(ASCP)SBB, Senior Technologist, Clinical Center Blood Bank

Other: Ritchard G. Cable, M.D., Assistant Resident, Blood Services Section, Clinical Center Blood Bank
William D. Terry, M.D., Associate Director, Immunology Branch, DCBD, NCI
Richard J. Hodes, M.D., Head, Immunology Section, Immunology Branch, DCBD, NCI
Susan Gross, R.N., Immunotherapy Research Nurse, Immunology Branch, DCBD, NCI

COOPERATING UNITS (if any)
NCI

LAB/BRANCH
Blood Bank Department

SECTION
Blood Services Section

INSTITUTE AND LOCATION
Clinical Center, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.5 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

On routine testing, it was discovered that two patients with malignant melanoma had developed the red blood cell antibody, anti-Chido(Ch$^a$), following the initiation of cancer immunotherapy in the treatment of their disease. We are currently testing the Ch$^a$ antigen status of the remaining persons in this protocol to see if the number varies from the statistical norm of 98% Ch$^a$ positive. We are attempting to test the Ch$^a$ antigen status of three cell lines of neuraminadase treated and untreated cultured melanoma cells used for injection in this protocol to determine if these cells can be responsible for inducing antibody production.

Serial No. Z01-CL-02012-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Chido(Ch$^a$) Antibody Production Induced by Cancer Immunotherapy

Previous Serial Number: Z01-CL-02012-02-BB

Principal Investigator: Mary L. Gustafson, MS, MT(ASCP)SBB

Other Investigators: Ritchard G. Cable, M.D.
Edwin J. Matthews, Ph.D.
Lloyd L. Lauer, M.S.

Cooperating Units: Inside NIH
NCI

Outside NIH
Litton Bionetics, Inc.

Man Years: Total: 0.5
Professional: 0.5
Other: 0

## Project Description

### Objectives:

To determine the Ch$^a$ antigen status of the cell lines used in the treatment of persons with malignant melanoma to determine whether these cells are responsible for inducing antibody production.

### Methods Employed:

Ch$^a$ antigen status of individuals is determined by a serum agglutination inhibition procedure. Absorption-elution techniques will be employed in the experimental testing for the Ch$^a$ antigen on the neuraminadase treated and untreated melanoma cells from culture.

### Major Findings:

To date, one other person on the melanoma therapy protocol appears to be Ch$^a$ negative.

Significance to Biomedical Research and the Program of the Institute:

This may demonstrate the first evidence of red blood cell antibody production following treatment of cancer immunotherapy.

Proposed Course:

See objectives and methods.

Publications:

Gustafson, M., Cable, R.G., Matthews, E.J., Lauer, L.L., Holland, P.V.: Anti-Chido Following Cancer Immunotherapy. Abstract Book, 30th Annual AABB Meeting, Atlanta, 1977.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02013-03 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Mechanism of Vertical Transmission of Hepatitis B Virus

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: George Grady, M.D.

Others: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank Department, Clinical Center

COOPERATING UNITS (if any)
Mass. Department of Public Health

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Maternal-fetal transmission is felt to be responsible for a large number of chronic carriers of HBsAg. The mechanism by which the virus is transmitted from mother to infant, is, however, unclear with the three main possibilities being: (1) transplacental transmission prior to birth (2) swallowing of maternal blood at the time of delivery and (3) post partum transmission via breast feeding or maternal handling.

We will attempt to sort these possibilities by delivering the infants of HBsAg-positive chimpanzees by Caesarian section and by having the infant reared separate from the HBsAg-positive mother.

Serial No. Z01-CL-02013-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

NIH-PHS
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Mechanism of Vertical Transmission of Hepatitis B Virus

Previous Serial Number: Z01-CL-02013-02 BB

Principal Investigator: George Grady, M.D.

Other: Harvey J. Alter, M.D., CCBBD

Cooperating Units: Massachusetts Dept. of Public Health

Man Years: Total: 1
Professional: 0.5
Other: 0.5

## Project Description

1. To see if maternal-fetal hepatitis transmission occurs despite the absence of any post-partum contact between mother and infant.
2. To see if the possibility of blood ingestion by the fetus can be avoided by bloodless Caesarian section and to see what impact this has on maternal-fetal transmission.
3. To see if prepartum transmission can be documented by the presence of HBsAg in cord blood or by the presence of hepatitis related antigens in fetal liver tissue obtained at the time of delivery.

## Methods:

1. Chronic HBsAg carrier chimpanzees will be housed and bred in the Labatory for Experimental Medicine and Surgery (LEMSIP). The carriers employed will be e antigen positive to document their potential infectivity.
2. Chimps will be delivered by as atraumatic and bloodless Caesarian section as possible.
3. At birth, samples will be obtained for HBsAg and e antigen testing from maternal blood, cord blood, fetal venous blood and amniotic fluid. A liver biopsy will also be obtained from the fetus and stained by fluorescent techniques for the presence of HBcAg and HBsAg.

4. The fetus will have no contact with the HBsAg-positive mother after delivery and will be followed for the development of type B hepatitis.

Major Findings:

The first infant so studied developed type B hepatitis seven weeks after delivery. This rules out post-partum contact as the cause of hepatitis transmission, but does not distinguish the other possibilities because the Caesarian section was not entirely bloodless. Against transplacental transmission, was the finding of HBsAg-negative cord blood and fetal venous blood. However, liver biopsy was not performed at the time of birth.

Significance to Biomedical Research and the Program of the Clinical Center:

It has been estimated that maternal-fetal transmission of hepatitis B may be the major cause for the development of the HBsAg carrier state. Throughout the world this is probably a far more significant route of transmission than blood transfusion. Any studies which elucidate the mechanism of such transmission may help in its prevention. It has already been proposed that mothers who are HBsAg-positive be delivered by Caesarian section. These studies may shed light on the rationale for such an approach.

Proposed Course:

The carrier mother whose fetus has already been followed will be inpregnated as soon as possible and the second fetus delivered by a more meticulous C-section and also biopsied at the time of delivery.

Publications: None

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01-CL-02014-03 BB

PERIOD COVERED

October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Transmission of Non-A, Non-B Hepatitis to Chimpanzees

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section,
Blood Bank Department, CC

Other: Robert Purcell, M.D., NIAID
Paul V. Holland, M.D., CCBBD

COOPERATING UNITS (if any)

NIAID

LAB/BRANCH

Blood Bank Department

SECTION

Immunology Section

INSTITUTE AND LOCATION

Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Ninety percent of post-transfusion hepatitis now appears related to a third human hepatitis "virus" tentatively termed "non-A, non-B." There are several pieces of evidence to suggest this is a virus but to date this agent has not been observed, has not had an identifiable antigenic marker, has not been grown in culture and has not been transmitted to animals. This study will attempt to identify bloods with a high probability of containing virus and will then attempt chimpanzee inoculation. If chimpanzees are infected, they will be observed for the development of chronic hepatitis, will be reinoculated to stimulate antibody responses and will be cross challenged to determine if there is more than one non-A, non-B agent.

PHS-6040
(Rev. 10-76)

Serial No. Z01-CL-02014-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Transmission of Non-A, Non-B Hepatitis to Chimpanzees

Previous Serial Number: Z01-CL-02014-02 BB

Principal Investigator: Harvey J. Alter, M.D.

Other: Robert Purcell, NIAID
Paul V. Holland, CCBBD

Cooperating Units: NIAID

Man Years: Total: 3
Professional: 1.5
Other: 1.5

## Project Description

Objectives:

1. To prove that non-A, non-B hepatitis is due to a transmissable agent.
2. To transmit this agent from human blood to chimpanzees and if successful from chimpanzee to chimpanzee.
3. To obtain plasmapheresis units from infected chimpanzees to aid in characterization of the virus and development of serologic tests.
4. To determine if more than one agent of non-A, non-B hepatitis exists.

Methods:

1. Potentially infectious sera will be obtained from patients with acute and chronic non-A, non-B hepatitis and from donors implicated in such transmission.
2. Depending on the volume of sample available, either 1 ml or 75 ml will be inoculated into chimpanzees and the animals followed for six months for evidence of enzyme (SGOT/SGPT) elevations.
3. Animals with elevated SGOT/SGPT will be plasmapheresed and have liver biopsies. Biopsy material will be observed for evidence of hepatitis, and will also be examined by immunofluorescence and electronmicrography.

4. Acute phase plasma from reactive chimps will be administered to additional animals in an attempt to demonstrate serial passage.
5. Infected chimps will be rechallenged with the same inoculum to boost antibody response.
6. Following 5, chimpanzees will be cross challenged to determine by cross immunity if there is more than one agent of non-A, non-B hepatitis.
7. Partial hepatectomy may be performed in infected chimps to serve as a source of non-A, non-B antigen.

Major Findings:

Sera were obtained from four patients with well documented non-A/non-B hepatitis and from one donor implicated in non-A/non-B transmission. These were inoculated into five chimpanzees and all five showed biochemical and histologic evidence of acute hepatitis. This study demonstrated two major points: (1) non-A/non-B hepatitis is due to a transmissible agent (2) there is a chronic carrier state in humans for the non-A, non-B agent(s) just as there is for the type B agent. The later is based on the fact that transmission occurred following inoculation of plasma obtained from patients with chronic as well as acute non-A/non-B hepatitis.

Three serial passages have been documented in chimpanzees. Booster experiments have been done but the samples have not been analyzed for antibody.

Proposed Course:

Additional chimps may be inoculated using sera derived from patients whose incubation period suggests a second non-A, non-B agent. Cross challenge experiments will also proceed in an attempt to define if there is more than one non-A, non-B agent.

Publications:

1. Alter, H. J., Purcell, R.H., Holland, P.V. and Popper, H.: Transmissible Agent in "Non-A, Non-B" Hepatitis. Lancet 1: 459-463, 1978.
2. Shimizu, Y.K., Feinstone, S.M., Purcell, R.H., Alter, H.J., and London, W.T.: Non-A, Non-B hepatitis: Ultrastructural evidence for Two agents in Experimentally Infected Chimpanzees. Science 205: 197-200, 1979.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02016-03 BB |
|---|---|---|

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Evaluation of Anti-Core Antibody and Serum Transaminase as Indicators of the Infectivity of HBsAg-Negative Donors

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank Department, Clinical Center

Other: Paul V. Holland, M.D., Chief, Blood Bank Department, CC
Deloris Koziol, Medical Research Technologist, Blood Bank Department, Clinical Center

COOPERATING UNITS (if any)

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 0.5 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Despite sensitive radioimmunoassay tests for HBsAg applied to all donor blood, some type B hepatitis continues to occur following transfusion. It has previously been suggested that HBsAg negative individuals that have anti-core antibody may transmit the hepatitis B virus. The availability of a new sensitive radioimmunoassay for anti-core antibody allows this postulate to be tested in our prospectively followed, open heart surgery patients. Similarly, we can ascertain if chronic carriers of non-A, non-B hepatitis have elevated serum transaminase; and, if so, whether this could be employed to screen donors and reduce the frequency of post-transfusion hepatitis due to this agent.

Serial No. Z01-CL-02016-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Evaluation of Anti-Core Antibody and Serum Transaminase as Indicators of the Infectivity of HBsAg-Negative Donors

Previous Serial Number: Z01-CL-02016-02 BB

Principal Investigator: Harvey J. Alter, M.D.

Other: Paul V. Holland, M.D.
Deloris Koziol, Medical Research Technologist

Cooperating Units: None

Man Years: Total: 1.5
Professional: 0.5
Other: 1

## Project Description

### Objectives:

1. To determine if HBsAg-negative donors who have anti-core antibody are more likely to transmit type B hepatitis than those who lack anti-core antibody.

2. To determine if donors with elevated SGPT are more likely to transmit non-A, non-B hepatitis than donors with normal SGPT and to ascertain if this would be a practical way to screen for chronic carriers of this presumed virus.

### Methods:

1. We have now prospectively followed over 400 patients to determine if they developed post-transfusion hepatitis and, if so, by what etiologic agent. All donors to type B and non-A, non-B hepatitis cases will be tested for anti-core antibody as will the donors to at least 30 patients who did not develop hepatitis (approximately 500 donors in all). Data will be analyzed to see if there is any positive correlation between the presence of anti-core antibody in the donor and hepatitis in the recipient.

2. All donors to open heart surgery patients will be tested for SGPT. These tests will be performed in a sample obtained at the time of donation but,

will not be tested until approximately three days after transfusion. The results of transaminase tests will not be known at the time of transfusion, but recipients will be followed prospectively for the development of hepatitis. Data will be analyzed to see if there is a positive correlation between the presence of elevated donor transaminase and the development of recipient hepatitis.

3. When an elevated transaminase is found (initially tested under contract by Bionetics Lab), the same sample will be retested by the Clincial Chemistry lab at NIH. If the elevated value is confirmed and hepatitis occurs in the recipient, the donor will be recalled and at least two units of plasma obtained by plasmapheresis for subsequent attempts to isolate a non-A, non-B agent.

**Major Findings:** None to date

### Significance to Biomedical Research and the Program of the Clinical Center

Any test system which could reliably detect carriers of hepatitis B who are below the detectability range of RIA tests for HBsAg or which would detect chronic carriers of non-A, non-B virus would have major impact on the incidence of post-transfusion hepatitis.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02017-03-BB |

PERIOD COVERED
October 1, 1978 to September 30, 1979

TITLE OF PROJECT (80 characters or less)
Identification of the Non-A, Non-B Hepatitis Agent and the Development of Serologic Markers

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., CCBBD

Others: Robert Purcell, M.D., NIAID
Stephen Feinstone, M.D., NIAID
John Gerin, Ph.D., Georgetown University

COOPERATING UNITS (if any)

Laboratory Infectious Disease, NIAID
Georgetown University

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A/1E33, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A non-A, non-B antigen will be sought in serum from patients with acute or chronic non-A, non-B hepatitis by reacting them with convalescent phase serum in a solid phase radioimmunoassay. In addition, plasma units derived from: either donors implicated in non-A, non-B hepatitis or patients with acute or chronic non-A, non-B hepatitis will be ultracentrifuged. The pellet derived by ultracentrifugation will be reacted against a radiolabelled IgG fraction obtained from patients convalescent from non-A, non-B hepatitis in a solid phase radioimmunoassay system.

Z01-CL-02017-03-BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Identification of the Non-A, Non-B Hepatitis Agent and the Development of Serologic Markers

Previous Serial Number: Z01-CL-02017-02-BB

Principal Investigator: Harvey J. Alter, M.D.

Others: Robert Purcell, NIAID
Stephen Feinstone, NIAID
John Gerin, Georgetown University

Cooperating Units: NIAID, Georgetown University

Man Years: Total: 2
Professional: 1
Other: 1

## Project Description

### Objectives:

1. To obtain a large quantity of non-A, non-B viral antigen.
2. To establish a sensitive detection system for this presumed viral agent.

### Methods:

1. Semi-purify non-A, non-B viral antigen by ultracentrifugation of plasma units clinically presumed to carry this agent.
2. Prepare radiolabelled IgG from plasma of persons who have recovered from non-A, non-B hepatitis in the hopes that they contain specific antibody.
3. React the antigen and antibody in a solid phase radioimmunoassay system.
4. If an assay can be developed, the antigen pellet will be further purified by cesium chloride and sucrose gradients.

## Major Findings:

Five plasma units have thus far been ultracentrifuged and found negative. Additional plasma units will be investigated as will acute and chronic phase serum samples.

**Proposed Course:** See objectives and methods

## Significance to Biomedical Research and the Program of the Clinical Center

The development of a detection system for non-A, non-B viral agent(s) would be highly significant in that none are currently available and in that this agent(s) currently is responsible for over 90% of posttransfusion hepatitis and probably responsible for a great deal of chronic active hepatitis.

**Publications:** None

| | | |
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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>ZO1-CL-02018-03-BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Hepatitis B Vaccine Trial Among Renal Dialysis Patients

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Wolf Szmuness, M.D., Chief, Epidemiology,
New York Blood Center

Other: Cladd Stevens, M.D., NYBC
Edward Harley, NYBC
Harvey J. Alter, M.D., CCBB

COOPERATING UNITS (if any)

New York Blood Center

LAB/BRANCH
Blood Bank Department

SECTION

Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 6 | 2 | 4 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A two part study is being undertaken to evaluate a hepatitis B vaccine being produced by NIAID. In the first phase baseline seroepidemiologic data will be obtained in 10 dialysis units in NYC and the Metropolitan Washington Renal Dialysis Unit. When the hepatitis B vaccine is available (approximately Fall 1979) a prospective, controlled, randomized double blind trial of its efficacy will be undertaken in these same dialysis units.

Serial No. ZO1-CL-02018-03-BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Hepatitis B Vaccine Trial Among Renal Dialysis Patients

Previous Serial Number: ZO1-CL-02018-02-BB

Principal Investigator: Wolf Szmuness, M. D.

Other: Cladd Stevens, M.D., NYBC
Edward Harley, NYBC
Harvey J. Alter, M.D., CCBBD

Cooperating Units: New York Blood Center

Man Years: Total: 6
Professional: 2
Other: 4

## Project Description

### Objectives:

1. To obtain baseline incidence figures on hepatitis B and non-A, non-B among a large number of renal dialysis patients and staff.

2. To try to assess patterns of hepatitis spread in these units based on serologic and epidemiologic parameters.

3. To evaluate the effectiveness of a hepatitis B vaccine in reducing the frequency of type B hepatitis among patients and staff.

### Methods:

1. Patients and staff in multiple dialysis units will be monitored monthly for evaluation of SGPT and appearance of HBsAg and anti-HBs. More frequent sampling and additional tests such as those for subtyping, e antigen and anti-core antibody will be employed when a positive result is obtained.

2. When the hepatitis B vaccine is ready for clinical trials, patients and staff of these dialysis units will be randomly assigned to receive hepatitis B vaccine or placebo and the effectiveness of each assessed over a one year period in each individual. The hepatitis B vaccine will be prepared from a purified preparation of 20 nm HBsAg-containing par-

ticles which have been formalin treated and which have already been shown to be non-infectious, but immunogenic, in chimpanzees. Patients and staff will be monitored as above.

3. Other potential methods of decreasing the risk of hepatitis will also be employed including the administration of HBIG to those accidentally inoculated with HBsAg-positive material and the isolation of postitive patients as recommended by the CDC.

4. All serologic and epidemiologic data will be computerized.

Major Findings:

Study is just in preliminary phase and sufficient data have not be accumulated for analysis.

Significance to Biomedical Research and the Program of the Clinical Center

Dialysis patients and staff remain a very high risk population for hepatitis B and represent one of the few US populations in which a hepatitis vaccine can be clinically evaluated. If the vaccine proves effective, it will have vast implications, not only for dialysis patients and staff, but also for patients and staff in institutions, for medical personnel in general, for inner city and sexually promiscuous populations, and for many foreign populations where hepatitis B frequencies are extremely high.

Proposed Course: See methods and objectives.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-02019-03 BB |

PERIOD COVERED

October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Evaluation of the hepatitis risk of hospitalized patients undergoing invasive procedures, but not receiving blood transfusion

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principle Investigator: Harvey J. Alter, M.D., Chief, Immunology Section,
Blood Bank Department, Clinical Center

Other: Paul V. Holland, M.D., Chief, Blood Bank Department, CC
Robert H. Purcell, M.D., Head, Hepatitis Virus Section, LID, NIAID

COOPERATING UNITS (if any)

NIAID, NHLBI

LAB/BRANCH

Blood Bank Department, Clinical Center

SECTION

Immunology Section

INSTITUTE AND LOCATION

Clinical Center, Building 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>3.5 | PROFESSIONAL:<br>0.5 | OTHER:<br>3 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This is a new study which will serve to supplement and control project Z01-CL-02005-10 BB. Cardiac patients will be enrolled if they undergo closed mitral commissurotomy or cardiac catheterization but do not receive blood. They will then be followed prospectively for 6 months and hepatitis rates compared with patients undergoing open heart surgery. This should provide data on the relative risk of hepatitis between transfusion exposure and exposure to a hospital environment and the types of hepatitis associated with each.

Serial No. Z01-CL-02019-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Evaluation of the hepatitis risk of hospitalized patients undergoing invasive procedures, but not receiving blood transfusion

Previous Serial Number: Z01-CL-02019-02 BB

Principal Investigator: Harvey J. Alter, M.D.

Other: Paul V. Holland, M.D.
Robert H. Purcell, M.D.

Cooperating Units: NIAID, NHLBI

Man Years: Total: 3.5
Professional: 0.5
Other: 3

## Project Description

### Objectives:

1. To determine if there is a viral hepatitis risk which accompanies hospitalization and invasive procedures such as closed mitral commissurotomy and cardiac catheterization.

2. To compare this hepatitis risk with patients with similar cardiac lesions who require transfusion as part of corrective surgical procedures for their cardiac lesion.

3. To determine the type of viral hepatitis in each group (i.e. B versus non-A, non-B) and thus to establish the absolute incidence of non-A, non-B hepatitis related to blood transfusion.

### Methods:

1. All patients undergoing closed mitral commissurotomy or cardiac catheterization (with or without coronary angiogram) will be followed for six months with serial tests for SGPT, HBsAg and anti-HBs.

2. Cases who develop hepatitis will be additionally tested for serologic responses to CMV, EBV and the hepatitis A virus; if type B disease, they will be additionally tested for anti-core antibody, e antigen and will be subtyped.

Major Findings: Study just beginning but 60 subjects enrolled to date.

Significance to Biomedical Research and the Program of the Clinical Center

This study will serve as a control for project no. Z01-CL-02005-10 BB and will define the baseline hepatitis incidence which accompanies hospitalization and invasive procedures not accompanied by blood transfusion.

Proposed Course: See objectives and methods

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02020-03-BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Alterations in Whole Blood Oxygen Affinity Following Transfusion

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey G. Klein, M.D., Chief, Blood Services Section, Blood Bank Department, CC

Other: Robert M. Winslow, M.D., Senior Investigator, National Heart Lung and Blood Institute

COOPERATING UNITS (if any)
NHLBI

LAB/BRANCH
Blood Bank Department

SECTION
Blood Services Section

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 2 | PROFESSIONAL: 1 | OTHER: 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It has been widely reported that whole blood oxygen affinity varies in different disease states characterized by anemia. The fact that whole blood oxygen affinity is reduced in persons with sickle cell anemia has been known for many years. A recent report indicates that non-transfused children with homozygous B thalassemia may have a paradoxical increase in anemia. There is very little quantitative information concerning serial changes in whole blood $O_2$ affinity posttransfusion in those disease states which require transfusion of red cells. It is quite possible that posttransfusion changes in $O_2$ affinity actually result in a more severe functional anemia despite the hemoglobin elevation. If the red cell milieu is important, as the report concerning thalassemia major suggests, whole blood $O_2$ affinity posttransfusion may differ significantly in such different disease states as thalassemia, sickle cell anemia, aplastic anemia and myeloid metaplasia. In this study, whole blood $O_2$ affinity will be measured in patients who require transfusion (1) prior to transfusion (2) daily for 5 days (3) weekly thereafter for three weeks. Whole blood oxygen affinity of the transfused blood will be measured as well. A quantitative estimate of the percent of transfused cells remaining in each sample will be derived by differential agglutination (Ashby technique).

PHS-6040
(Rev. 10-76)

Serial No. Z01-CL-02020-03-BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Alterations in Whole Blood Oxygen Affinity Following Transfusion

Previous Serial Number: Z01-CL-02020-02-BB

Principal Investigator: Harvey G. Klein, M.D.

Other: Robert M. Winslow, M.D.

Cooperating Units: NHLBI

Man Years: Total: 2
Professional: 1
Other: 1

## Project Description

### Objectives:

1. Determine what alterations occur in whole blood oxygen affinity and 2,3 DPG following transfusion.

2. Determine whether any changes in oxygen affinity occur in the transfused red cells which might suggest an influence of the "disease milieu."

3. Determine whether such changes vary according to the blood product transfused (fresh blood, bank blood, frozen blood).

4. Follow these alterations as the transfused red cells are eliminated from the recipient's circulation.

5. Exercise patients pre- and posttransfusion to determine physiological correlation with changes in $O_2$ affinity.

### Methods Employed:

This study will be carried out over a two year period. Patients who require transfusion on the Molecular Hematology Service will be studied. The studies will initially be confined to patients with thalassemia, sickle cell anemia and aplastic anemia. Initially patients of blood group A, B, or AB will receive group O ("universal donor") packed red cells. A five cc pretransfusion specimen as well as a five cc aliquot from the transfused cells will be obtained for measurements of whole blood oxygen affinity and 2,3 DPG levels. Whole blood $O_2$ affinity will be measured by the technique of Rossi-Bernardi. A one hour posttransfusion specimen, daily specimen for five days and weekly specimens for three weeks will be drawn. Percent of transfused cells remaining will be measured by differential agglutination (Ashby technique) and correlated with changes in $O_2$ affinity. Additionally the recipient's cells will be lysed in-vitro by use of an anti-A or anti-B hemolysin. This will permit separation of transfused from recipient cells in the posttransfusion specimen. Oxygen affinity can then be determined directly on the remaining transfused cells and on the whole blood. These determinations permit calculation of $O_2$ affinity of the lysed recipient cells. In this way it should be possible to determine whether specific changes occur in the transfused cell population posttransfusion and what component is the major influence in changes in whole blood $O_2$ affinity.

A second series of studies using ABO identical transfusions of red cells and whole blood can be carried out if donor and recipient are not identical for a minor blood group. This is necessary to permit separation of donor from recipient cells following transfusion. For these studies, differences in the presence of red cell M antigen will be used to distinguish donor from recipient cells. This antigen was chosen because of its low antigenicity, rarity of clinical importance of anti-M isoantibodies, and presence of an anti-M reagent potent enough to effect the required separation.

## Major Findings:

In sickle cell disease, changes in flow characteristics which result from exchanging AA cells for SS cells are more important in determining $O_2$ delivery than are shifts in the oxygen dissociation and 2,3 DPG levels.

## Significance to Biochemical Research and the Program of the Clinical Center

This project has practical importance in the management of blood resources and the transfusion approach for chronic anemia. Results of these studies should indicate the physiologic changes that result in different anemia states when various red cell preparations are transfused.

## Proposed Course:

This study should have its initial phase completed within one year.

Publications: none

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02022-02 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Identification of Bacterial Organisms with human red cell antigen specificity.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigators: Mary H. McGinniss, AB(ASCP)SBB
Research Biologist
Paul V. Holland, M.D., CCBBD Chief

Other: James D. MacLowry, M.D. CC, CP, Deputy Chief

COOPERATING UNITS (if any)

Clinical Pathology

LAB/BRANCH
Microbiology

SECTION

INSTITUTE AND LOCATION
Clinical Center, Building 10

| | | |
|---|---|---|
| TOTAL MANYEARS: 2 | PROFESSIONAL: 2 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Bacterial organisms are being analyzed for inhibitory property for red cell antibody and ability to confer red cell antigens on red cells negative for those antigens.

The red cells of patients with positive blood cultures are being analyzed for acquisition of non-genetically determined red cell antigens.

PHS-6040
(Rev. 10-76)

Serial No. Z01-CL-02022-02 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Identification of bacterial organisms with human red cell antigen specificity

Previous Serial Number: Z01-CL-02022-01-BB

Principal Investigators: Mary H. McGinniss, AB(ASCP)SBB
Paul V. Holland, M.D.

Other: James D. MacLowry, M.D.

Cooperating Units: Inside NIH
Microbiology Service, Clin. Path. Dept., CC

Outside NIH
None

Man Years: Total: 2
Professional: 2

## Project Description

### Objectives:

A. To identify bacteria with red cell antigen-like specificity.

C. To search for acquisition of non genetic antigens in septicemic patients.

### Methods Employed:

1. Bacterial cultures, whole and sonicated, plus their filtrates are being analyzed for their ability to inhibit antibodies and adsorb to human red blood cells.

2. Patients with bacterially proven sepsis will have their red cells phenotyped for the presence of non-genetic red cell antigens. This will require phenotype of pre-sepsis red cells and/or phenotype of family members, if available.

### Major Findings:

One patient, with D-strep sepsis, developed an acquired Kell antigen. Sonicated organisms from this patient had the ability to turn Kell negative cells, Kell positive in-vitro and the whole organisms turned JK(b-) cells to JK(b+).

Another patient, with P. mirabilis infection, made an auto anti-JKb causing a brisk hemolysis in-vivo. P. mirabilis organisms will confer JKb-like specificity to JK(b-) cells in-vitro.

Significance to Biomedical Research and the Program of the Institute:

A. Elucidation of a previously known phenomenon by which patients may develop allo or auto antibodies to red cell antigens which may restrict the availability of crossmatch compatible blood.

B. Biochemical analysis of organisms with specificity similar to red cell antigens may aid in understanding the biochemistry of single red cell antigen specificities.

C. Understanding of red cell antigens in health and disease whereby these usually genetically controlled characteristics may be lost or acquired in certain clinical situations.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-02023-02 BB |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Blood Group Substances in Malignant and Benign Breast Cyst Fluids

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Mary H. McGinniss AB(ASCP)SBB
Research Biologist Clinical Center Blood Bank

Other: Ernest V. DeMoss, M.D., Surgical Branch, NCI

COOPERATING UNITS (if any)

NCI

LAB/BRANCH
Surgical Branch, NCI

SECTION

INSTITUTE AND LOCATION
Clinical Center, Bldg. 10, NCI

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>1 | PROFESSIONAL:<br>1 | OTHER:<br>0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Breast cyst fluids are being analyzed for the presence of soluble blood group substances, both serologically and biochemically. These data will be correlated, at a later date, with breast cyst fluid analysis for malignancy. If a consistent difference is noted between malignant and non-malignant cyst fluids, it may serve as a marker for patients at risk.

PHS-6040
(Rev. 10-76)

Serial No. Z01-CL-02023-02 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Blood Group Substances in Malignant and Benign Breast Cyst Fluids

Previous Serial Number: Z01-CL-02023-01-BB

Principal Investigator: Mary H. McGinniss, AB(ASCP)SBB

Other Investigators: Ernest V. DeMoss, M.D.

Cooperating Units: Inside NIH
NCI

Outside NIH
None

Man Years: Total: 1.0
Professional: 1.0
Other: 0

## Project Description

Objectives:

A. To delineate any differences in soluble blood substances found in breast cyst fluid from malignant tissue as opposed to benign tissue.

B. To test the accuracy of anti-T titers to predict breast malignancy as opposed to benign breast cysts.

Methods Employed:

1. Breast cyst fluids, supplied by Dr. DeMoss of the NCI Surgical Branch, will be tested, using an inhibition test, for the presence or absence of $Le^a$, $Le^b$, A, B, H, M, N and T soluble substances.

2. Blood serum from the patients will be tested for atypical red cell antibodies and anti-T titer.

3. Saliva from these patients will be tested for secretor status (ABH) and Lewis substance.

4. Red cells will be used for a complete red cell phenotype.

Major Findings:

Cyst fluid from 16 patients have been studied. Three fluids appeared to inhibit an anti-T reagent. One patient had a significantly low titer of anti-T in her serum and her cyst fluid partially inhibited the anti-T reagent. Serum has not been obtained yet on two of the three patients whose cyst fluid inhibited the anti-T reagent. The third had a normal anti-T titer.

Work is continuing using a modification of the method used to date for cyst fluids. Cyst fluids will now be boiled to destroy enzymes which may inactivate blood group substances and they will also be filtered to render them free of cellular debris. These data will be correlated soon with cytology data. Work will continue until 50 patients' cyst fluids have been analyzed.

Significance to Biomedical Research and the Program of the Institute:

A. If a consistent difference is noted between malignant and nonmalignant cyst fluids, it may serve as a marker for patients at risk.

B. Anti-T titers could become part of a breast cancer work-up.

Proposed Course:

To analyze, as stated above, 50 patients who are admitted for aspiration of breast cyst fluid.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br><br>Z01-CL-02024-02-BB |

PERIOD COVERED

October 1, 1978 - September 30, 1979

TITLE OF PROJECT (60 characters or less)

Frozen Red Cells in Prevention of Non-A/Non-B Hepatitis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., CCBB

Other: Robert Gerety, BOB, FDA
Leonard Seeff, VA, Wash., D.C.
George Grady, State Lab, Boston, Mass.

COOPERATING UNITS (if any)

VA Hospital, Washington, D.C.
State Lab, Boston, Mass.

LAB/BRANCH

Blood Bank Department, Clinical Center; Bureau of Biologics, Bethesda, MD.

SECTION

Immunology Section

INSTITUTE AND LOCATION

Clinical Center, Building 10A/1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>3 | PROFESSIONAL:<br>1 | OTHER:<br>2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It has been suggested in the literature, but never conclusively documented, that frozen-deglycerolized red cells (FDRC) could prevent post-transfusion hepatitis (PTH). In a recent experiment, we showed in a chimpanzee model that FRBC did not prevent the development of type B PTH. Since 80-90% of PTH is now due to the non-A/non-B agent or agents it seems appropriate to determine if FRBC play any role in prevention of this disease. Such a study has now become feasible because of the recent transmissions of non-A/non-B hepatitis to chimpanzees. In this study, we will utilize whole blood from a donor shown to transmit non-A, non-B hepatitis to both humans and chimpanzees. The blood will be frozen and deglycerolized by standard techniques and then tested for infectivity in chimpanzees.

PHS-6040
(Rev. 10-76)

Serial No. ZO1-CL-02024-02-BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Frozen Red Cells in Prevention of Non-A/Non-B Hepatitis

Previous Serial No.: ZO1-CL-02024-01-BB

Principal Investigator: Harvey J. Alter, M.D.

Other: Robert Gerety, BOB, FDA
Leonard Seeff, M.D., VA, Washington, D.C.
George Grady, M.D., State Lab, Boston, Mass.

## Project Description

1. To procure whole blood units known to contain an infectious inoculum of the non-A/non-B hepatitis agent.

2. Units will be subjected to a standard method of freezing and deglycerolization.

3. Frozen and deglycerolized cells and appropriate controls will be inoculated into chimpanzees who will be followed for biochemical and histologic evidence of viral hepatitis.

## Methods:

1. Whole units of blood will be obtained from a donor known to transmit non-A/non-B hepatitis. In addition, a large volume of infectious plasma will be obtained by plasmapheresis.

2. Freezing and deglycerolization will be performed by a standard procedure for human use employing the IBM red cell washer.

3. Chimpanzees will be transfused with frozen deglycerolized cells and followed with weekly SGOT/SGPT. Biopsies and plasmapheresis units will be obtained when indicated.

4. Chimpanzees who do not become infected will be tested for susceptibility to the non-A/non-B agent by subsequent inoculation with the untreated infectious plasma pool.

Major Findings: None to date

Proposed Course: See Objectives

## Significance to Biomedical Research and the Program of the Institute

There is considerable uncontrolled data in the literature to suggest that FRBC prevent PTH. If true, this would provide a means of preventing PTH irrespective of our ability to detect virus in the donor. However, a previous chimpanzee study in our laboratory demonstrated that FRBC did not prevent type B PTH. Since 80-90% of posttransfusion hepatitis is now classified as non-A/non-B, it is important to establish if freezing and deglycerolization might prevent this form of hepatitis.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>ZO1-CL-02025-01-BB |

PERIOD COVERED

October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Chronic Tranfusion with a Fraction of Young Normal Red Cells (Neocytes)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigators: Harvey G. Klein, M.D., Chief, Blood Services Section, BBD, CC
Lawrence Corash, M.D., Hematology Section CPD, CC

Others: Arthur Nienhuis, M.D., Chief, Clinical Hematology Branch, NHLBI
Albert Deisseroth, M.D., Chief, Experimental Hematology Section, POB, NCI

COOPERATING UNITS (if any)

NHLBI and NCI

LAB/BRANCH

Blood Bank Department/Clinical Pathology Department

SECTION

Blood Services Section

INSTITUTE AND LOCATION

Clinical Center, Bldg. 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>2.5 | PROFESSIONAL:<br>1 | OTHER:<br>1.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The major complication of chronic red cell transfusion is hemosiderosis. One approach to limiting iron infusion is to lengthen the interval between transfusions. Although normal red cell survival is about 110 days, the average unit of blood contains cells of all ages, some of which survive only a few days post-transfusion. If one could prepare a unit containing only young red cells (neocytes), transfusion requirements might be halved. We have used an IBM 2997 cell separator to harvest a cohort of young cells of an average 15-30 days by by pyruvate kinase analysis. These cells are frozen and deglycerolized for transfusion into chronically transfused thalassemic patients. To date $^{51}$Cr survival data suggest that neocytes circulate up to twice as long as baseline frozen red cells. Clinical status of seven thalassemic patients, supported on neocytes for two years, will be monitored. Part II of this protocol involves removal of senescent red cells (gerocytes) by a similar cell separation technique.

Serial No. Z01-CL-02025-01-BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Chronic Transfusion with a Franction of Young Normal Red Cells (Neocytes)

Previous Serial No. None

Principal Investigator: Harvey G. Klein, M. D.
Lawrence Corash, M. D.

Other: Arthur Nienhuis, M. D.
Albert Deisseroth, M. D.

## Project Description

### Objectives:

1. Prepare frozen deglycerolized red cell units which contain red cells with an average of 15-30 days by pyruvate kinase assay.
2. Determine *in vivo* survival and function of these cells.
3. Follow the transfusion requirements of several chronically transfused patients whose baseline transfusion requirement is well established.
4. Determine the efficacy and practicality of using a continuous flow cell separator for partial exchange transfusion of selected fractions of red cells.

### Methods Employed:

1. Blood Bank donors are asked to undergo neocytopheresis on the IBM Cell separator, a procedure which lasts about four hours and results in the removal of approximately 50 gm of hemoglobin in a 500 ml. volume. Donors must pass all standards for both whole blood donation and plasmapheresis. The cell separator is adjusted to collect "neocytes", young red cells just below the buffy coat. Donor white cells, platelets and iron stores are monitored.
2. The neocyte component is frozen and assayed for pyruvate kinase before and after the freeze-thaw process. Such units are transfused into informed, chronically transfused, thalassemic patients who have had appropriate baseline studies. Seven such patients will eventually be totally supported by neocytes.

Significance to Biomedical Research and Programs of the Institute:

The Clinical Center has had a longstanding interest in the hazards of chronic transfusion and has supported the thalassemic patients studied for iron overload by the Clinical Hematology Branch, NHLBI. This protocol explores development of a new red cell component which should cut the danger of iron overload in chronically transfused patients by up to 50%. If the principle can be established, further technologic development could make this procedure a major step forward in chronic transfusion therapy.

Proposed Course:

The initial phase should last two years.

Publications: None

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-02026-01 BB |
|---|---|---|

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Immune Complexes in Non-A, Non-B Hepatitis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Jules Dienstag, M.D., Asst. Prof. of Medicine
Massachusetts General Hospital

Other: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD
Robert H. Purcell, M.D., Head, Hepatitis Virus Section, LID, NIAID

COOPERATING UNITS (if any)

NIAID

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A/Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3 | 2 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

1. Test sera from patients with non-A, non-B hepatitis for presence of immune complexes by RAJI cell assay and compare with patients with other forms of viral hepatitis and with controls without hepatitis.

2. Isolate complexes from non-A, non-B patients with high level activity by RAJI assay; dissociate complex and test derived "antigen" and "antibody" for non-A, non-B specificity by solid phase radioimmunoassay.

Serial No. Z01-CL-02026-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Immune Complexes in Non-A, Non-B Hepatitis

Previous Serial Number: None

Principal Investigator: Jules Dienstag, M.D.

Other Investigators: Harvey J. Alter, M.D.
Robert H. Purcell, M.D.

Cooperating Units: Inside NIH
NIAID

Outside NIH
Massachusetts General Hospital

Man Years: Total: 3
Professional: 2

## Project Description

### Objectives:

1. To determine if patients with non-A, non-B hepatitis have circulating immune complexes.
2. To isolate complexes by their attachment to RAJI cells.
3. To dissociate complexes in attempt to isolate specific antigen and/or antibody for non-A, non-B.
4. Test antigen and/or antibody by radioimmunoassay against appropriate acute and chronic hepatitis sera and against control sera.

### Methods:

1. Immune complexes will be measured by RAJI cell assay.
2. Immune complexes will be dissociated by low acid/or high molarity and the antibody reacted against sera by solid phase radioassay.

## Major Findings:

Immune complexes have been found in the majority of patients tested to date who are acutely ill with non-A, non-B hepatitis.

## Significance to Biomedical Research and the Program of the Institute:

There is a pressing need for a serologic test for the non-A, non-B virus(es). This project provides a novel approach to isolate a potential non-A, non-B antigen or antibody.

## Proposed Course:

See Objectives and Methods

## Publications:

Dienstag, J. L., Bhan, A. K., Alter, H. J., Feinstone, S. M., and Purcell, R. H.: Circulating Immune Complexes in Non-A, Non-B Hepatitis: Possible Masking of Viral Antigen. Lancet. i: 1265-1267, 1979.

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|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-MH0083-05 AP |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

Hypothesis of X-linkage in Bi-polar and Uni-polar Affective Disease

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Elliot Gershon, M. D., NIMH AP Branch

Other: Mary H. McGinniss, AB(ASCP)SBB, Research Biologist
Clinical Center Blood Bank

COOPERATING UNITS (if any)

Clinical Center Blood Bank

LAB/BRANCH
NIMH AP Branch

SECTION
Affective Disorders

INSTITUTE AND LOCATION
NIMH Clinical Center Building 10, Room 3N218

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It has been reported that one form of affective disease (manic-depressive disease) may be carried on the X chromosome. Phenotypes, including Xg typing, have been done on 200 patients representing a mixture of bipolar and unipolar diagnoses and 951 family members. This study ended December 31, 1978. Statistical data on Xg and the incidence of other blood group antigens are now being compiled.

Serial No. Z01-MH0083-05 AP
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 - September 30, 1979

Project Title: Hypothesis of X-linkage in Bi-polar and Uni-polar Affective Disease

Previous Serial Number: Z01-MH0083-04 AP

Principal Investigator: Elliot Gershon, M.D.

Other: Mary H. McGinniss, AB(ASCP)SBB

Man Years: Total: 2
Professional: 1
Other: 1

## Project Description

### Objectives:

A. To confirm or reject previously published claim that a gene involved in one form of manic depressive disease may be carried on the X sex chromosome.

B. By statistical analysis see if any correlation exists between manic depressive disease and any of the commonly known red cell antigens.

### Methods Employed:

1. Mental health evaluations and complete red cell phenotyping including Xg typing.

### Major Findings:

Six informative pedigrees were found. The reported linkage of Bi-polar major affective illness to known X-chromosomal markers, using the Xg blood group, could not be confirmed.

### Significance to Biomedical Research and the Program of the Institute:

See objectives

Publications:

"Studies of Xg and Bi-polar illness linkage" presented at the Annual APA meeting, May 1978 and paper entitled, "New data do Not Suggest Linkage between the Xg Blood Group and Bi-polar Illness," Gershon, E.S., Leckman, J.F., McGinniss, M.H., and Targum, S.D. is "in press" in Archives of Psychiatry.

NUCLEAR MED.

MED. REC.

CLIN. PATH.

ESCD

DIAG. RADIOL.

October 1, 1978 to September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## CLINICAL PATHOLOGY DEPARTMENT

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  B. Personnel....................CP-2
  C. Presentations....................CP-2
  D. Formal Training Courses Completed by Staff....................CP-2

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October 1, 1978 to September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH
CLINICAL CENTER

## CLINICAL PATHOLOGY DEPARTMENT

## I. DEPARTMENT MISSIONS AND GOALS

The Clinical Center Clinical Pathology Department missions and goals are:

1. To provide the optimum laboratory medicine support to patient-care physicians and their patients within the Clinical Center.

2. To act as a consultant to patient-care physicians regarding the interpretation of laboratory data and patient care problems in hematology.

3. To educate and train clinical pathology residents, clinical associates, and visitors in laboratory medicine.

4. To conduct a program of research and development in the area of laboratory medicine.

## II. DEPARTMENT ACTIVITIES

### A. Service Productivity

The Clinical Pathology Department performed 1,937,001 tests during FY-1979 which represents an 18.6% increase over FY-1978. The Resource Monitoring System average monthly workload index remained constant at 96 for both FY-78 and FY-79.

During the year, the Hematology Service has conducted a Wednesday morning Hematology Clinic which has been useful to channel large numbers of Clinical Center patients for hematology consultations, as well as patients referred to the Hematology Service for evaluation and hematologic procedures. The number of outpatient visits this year is greater than 400. The Hematology Clinic has been very successful and has allowed the Hematology Service to continue its major role as the hematology consultant to physicians and patients in the Clinical Center.

During the last year the Hematology Service has interpreted over 2400 bone marrow biopsies, clot sections, iron stains, and aspirate smears for patients in the Clinical Center. The number of specimens, which include biopsy and clot section as well as the regular smears, has increased remarkably requiring a great deal more time to interpret each bone marrow sample. A large number (250) of bone marrow specimens have been sent for consultation from within the National Cancer Institute, various surrounding institutions, as well as from all over the country.

NUCLEAR MED.
MED. REC.
FABRIC CARE
ESCD
DIAG. RADIOL.

During the last year the Hematology Service has interpreted over 2400 bone marrow biopsies, clot sections, iron stains, and aspirate smears for patients in the Clinical Center. The number of specimens, which include biopsy and clot section as well as the regular smears, has increased remarkably requiring a great deal more time to interpret each bone marrow sample. A large number (250) of bone marrow specimens have been sent for consultation from within the National Cancer Institute, various surrounding institutions, as well as from all over the country. This year the Hematology Service performed approximately 15% of the bone marrows in the Clinical Center.

The number of consultations in the Hematology Service this year increased to 37 patients per month. As in prior years, these consultations are not simply one physician visit but require multiple visits and follow-up of the patient for evaluation of laboratory results over a long period of time.

B. Personnel

Two Staff Fellows joined the Department this year, one in Hematology and the other in Microbiology.

C. Presentations

Fifty-one members of the Clinical Pathology Department made 70 formal presentations at universities and various national and international meetings.

D. Formal Training Courses Completed by Staff

Sixteen Commissioned Officers participated in 25 formal training courses.

Ninety-three Civil Service employees participated in 164 formal training courses.

III. Major Progress

A. Service

A revision of "The Clinical Pathology and Blood Bank Guide" was coordinated by the Office of the Chief. This guide is provided to help patient-care physicians make best use of laboratory services. It was distributed in August 1979, and contains a Master Table of all laboratory tests available at NIH whether performed by the Clinical Pathology Department, Blood Bank Department, laboratories within the Institutes, or via contract.

In January 1979, at the request of the Director of the Clinical Center, seven distinguished leaders in the field of laboratory medicine from around the country visited the Department for two days to evaluate the operations of the Department and make recommendations for improvement. The site visit team was headed by Dr. Morton Schwartz and included Drs. Norbert Tietz, Henry Isenberg, Thomas Gavin, Brian S. Bull, Klaus Mayer and G. Phillip Hicks. The site visit team submitted a 16-page report to the Director of the Clinical Center. Each Laboratory Chief in the Department commented on the report and several of the recommendations were implemented. The senior staff of the Department felt that this was a most constructive and worthwhile experience which has had many tangible benefits.

One of the recommendations made by the site visit team was to implement the workload unit system designed by the College of American Pathologists. Five members of the Department attended a two-day workshop on workload units given by the College in Arlington, Virginia. Part of the system has been implemented within the Department, and the entire system should be in place by the end of the calendar year. The self-inspection of the laboratories for the College of American Pathologists was conducted by two second-year residents. They noted a total of eight Phase II deficiencies which have been corrected.

The Phlebotomy and Urine Collection Service is fully staffed and also has two part-time (700 hour) members to assist at peak blood drawing times. The MIS computer request lists and labels are now used for in-patient phlebotomy. The phlebotomy pick-up team continues to pick up and deliver all specimens going to the clinical laboratories for analysis and to supply all patient-care areas with vacutainers. All blood cultures, gentamicin levels, and timed test specimens are a function of the Phlebotomy Team and have increased in volume. Services continue for sterile clean-catch urines which has resulted in better specimens for analysis and a decrease in the contamination rate.

The Clinical Chemistry Service added four new tests which previously had been obtained through contract laboratories, which will save over $75,000 per year. These four tests are the following: creatine kinase isoenzymes, 5'-nucleotidase and thyroid binding globulin serum, and 17-hydroxycorticosteroids in urine. In addition, the Service has been able to shorten considerably the turnaround time for each of these assays, especially important for creatine kinase isoenzymes, and has improved quality control by monitoring these tests directly. The following assays were considerably upgraded and improved: lipase, amylase, and urine urea nitrogen.

The Chemistry Service Procedure Manual has been completely revised, and all methods appear in a uniform format. These methods will now be updated at least annually by the senior staff.

A major renovation of the Chemistry Service was redistribution of the space for senior staff and expanding areas, such as radioimmunoassay and special chemistry.

A total review of personnel utilization, conducted by the Chief, Assistant Chief, and Chief Technologist of the Service, has resulted in a consolidation of the Microchemistry and Urinalysis Groups into one group which will increase the efficiency of the technical personnel. In addition, technical personnel were selected specifically for method development for each group. This will assist the Service with the scheduled development and implementation of assays which are now obtained through contract laboratories. Some of these assays may not be implemented until the move to the new laboratory in the Ambulatory Care Research Facility; however, plans have been made to reduce contracted tests to a minimum by 1982.

A program providing real-time analysis of quality control data generated by the SMAC multichannel biochemical analyzer has been developed and placed in operation on a PDP-11 computer interface to the SMAC.

Improvements of the electrophoretic technique to determine lactate dehydrogenase (LD) isoenzymes increased its specificity for the cardiac associated LD isoenzymes-1 and 2. This method has been evaluated and is successfully applied for the detection of myocardial infarction in patients undergoing cardiac operations.

The Service has performed glucose analyses on fluoridated plasma specimens for many years. An extensive study comparing paired serum and fluoridated plasma glucose values showed less than a 2 mg/dl difference per hour between the two specimens; as a result of this study, the Service has changed to serum for glucose analyses. This change saves several thousands of dollars per year in container and processing costs.

Continued efforts to improve our STAT/emergency laboratory services has led to a reduction in average turnaround time from 60 to 40 minutes.

An on-line computer link has been established between Herner Analytics, a major contract laboratory for the Department, and our Honeywell Computer System. Test results generated at Herner Analytics can now be entered directly into the laboratory computer system, thus speeding up their appearance on patient reports.

The Hematology Service continued to implement the program instituted last year which utilized whole blood samples rather than fingersticks for the majority of outpatient hematology determinations. This reduction in the number of fingersticks has continued through this year, and the number of fingersticks has been decreased to approximately 5% of that seen in previous years. The modification of the main hematology laboratory was completed and has allowed a shorter turnaround time for patient results to reach the patient-care physicians.

The Hematology Service adopted three new methods and the Coulter S Plus analytical system. The electro-immuno quantification for haptoglobin is more specific for this serum protein and will avoid toxic reagents used in the present method. A radioimmunoassay for the determination of both vitamin $B_{12}$ and folic acid on the same blood sample will be implemented in the near future. This method will reduce the amount of blood required for these determinations, reduce costs of outside contracts for folic acid determinations, and allow better clinical evaluation of these analytes by performing them simultaneously on the same specimen. The Coulter S Plus performs the seven components of the CBC in addition to a platelet count. After a thorough evaluation of this system, it was implemented and will provide a more rapid return of results to patient-care physicians, particularly platelet counts.

The Chief Medical Technologist of the Hematology Service, Ms. Minna Feld retired after a long and valuable service not only to the Hematology Service, but also to the Clinical Pathology Department and the Clinical Center. A new Chief Technologist, Mrs. Bettye Wages, was appointed. Furthermore, the Hematology Service was reorganized to include the areas of chemical hematology and immunologic hematology. The office of the Chief Technologist and the new chemical hematology group were moved to the first floor, adjacent to the Phlebotomy area to improve continuity of service.

The requesting and reporting of patient tests has been improved by the Laboratory Computer Service by establishing computer-to-computer links between the Clinical Pathology Department Honeywell laboratory computer system and the Clinical Center Technicon MIS computer. Requests for laboratory work are now received from MIS electronically. Test results are transmitted automatically to MIS and may now be retrieved throughout the hospital on MIS terminals. STAT and priority results are printed immediately and automatically in patient-care areas.

An interactive computer terminal linked to the Honeywell system has been installed at Herner Laboratories, a major contract laboratory for the Department. Herner Laboratories are now able to enter directly into the Honeywell system the results of those tests which they perform for the Department, making the results available sooner and reducing the clerical work required.

An improved format for presenting clinical laboratory results has been developed. The new reports group related tests together, present results in a cumulative chronological arrangement, and greatly reduced the number of pages required to summarize a patient's results.

The Microbiology Service has been designated by the Center for Disease Control as the U. S. reference laboratory for *P. aeruginosa* bacteriophage typing and serotyping. These techniques are important in the surveillance and epidemiology of hospital infections,

A number of laboratory procedures have been streamlined to eliminate unnecessary work, and the Service laboratory manuals have been extensively rewritten and reorganized to increase their clarity and utility.

The laboratory now has available the medium currently recommended for the isolation of Legionella pneumophila, the causative agent of Legionnaires' disease. All lung biopsy materials are planted onto this medium. Other specimens can be planted on specific request. In conjunction with this we are able to do direct fluorescent antibody screening using antisera for Legionella (serotypes Knoxville and Togas). This is done by specific request only.

A new anaerobic glove box was acquired in April 1979 which replaced an older model with which we had been having repetitive problems. The new glove-box has an automatic entry-port control which reduces the complexity of transporting items in and out of the chamber.

A modification of the stool occult blood procedure has been evaluated and implemented. This permits the laboratory to utilize non-carcinogenic agents, rather than benzidine hydrochloride, for this important screening procedure.

An automated method for the determination of total hemolytic complement has been evaluated and implemented. This will allow a much more rapid turnaround time for an otherwise very time consuming test procedure.

The use of the API-20C Mycology strip has been instituted for the more rapid identification of clinically significant yeasts.

Expanded use of the API-20E for non-fermenters has decreased the number of organisms for which longer, traditional techniques are needed for identification. Since we are now using API-20E for identification of non-fermentative Gram-negative rods, we have also set up a separate computer data acquisition file for storage and retrieval of the 9-digit codes for these organisms.

A rapid method for the identification of Neisseria species, particularly N. gonorrhoea and N. meningitidis, has been implemented. This method assesses carbohydrate utilization in one hour as opposed to the previous time of 24-48 hours.

A rapid slide agglutination procedure for streptococcal grouping has replaced the previously performed precipitin tube method using antigens extracted by the Rantz Randall procedure. This method allows the laboratory to provide grouping results more rapidly. Currently, two commercial grouping kits are being utilized in a comparative study.

Both an ASO titer and a Streptozyme multiple-enzyme slide test are being performed on all sera on which a request for streptococcal antibody determination is made. This provides a much broader screen for antibodies to streptococci and meets present CDC suggestions in this regard.

In December 1978 the Anaerobe Laboratory and Special Bacteriology Section was formed. This Section is responsible for anaerobe cultures as well as identification of unusual organisms submitted by the routine laboratory.

The Anaerobe Laboratory extended its service responsibilities to include anaerobic workup of all wounds and abscess specimens even if anaerobic culture was not specifically requested. This has improved the efficiency of isolation of anaerobes from these cultures and has streamlined the coordination of work between the routine and anaerobic laboratories.

The Microbiology Service continues to perform phage typing of *S. aureus* strains for outside hospitals along with this usual service to the Clinical Center.

The lyophilized bacterial culture collection continues to grow in numbers of cultures and requests for cultures from around the country.

B. Research and Development.

The *Office of the Chief* distributed a 14-page Pathology Questionnaire which evaluated the relationships between space, personnel, and test volume to over 100 academic pathology departments in the United States. Fifty departments completed the questionnaire. The data have defined mathematical relationships between space, personnel, test volume, publications, and budget that will be valuable to this Department and other pathology departments in the country. This information was presented at the Annual Meeting of the Academy of Clinical Laboratory Scientists and Physicians and is now being prepared for publication.

In the *Clinical Chemistry Service*, a variety of instruments were evaluated including a Hyland immunochemical system, several blood gas analyzers, and a new generation Micromedic automatic pipetting station. A number of analytical procedures were either upgraded or added to the laboratory as indicated above under Major Progress. The Service began assigning a medical technologist to each group to function as an R and D specialist for that area and to assist senior staff members in their research projects.

Work on applications of microcalorimetry continues. Calorimetric measurement of serum cholesterol and cholesterol ester on CDC control samples has been concluded.

Preliminary measurement of heat from antigen-antibody reactions using albumin as the antigen shows a correlation between the level of antigen and the amount of heat evolved. Further studies are required to analyze the thermogram pattern of these reactions.

The project investigating the application of the radioimmunoassays for isoenzymes MM and BB of creatine kinase to patients with schizophrenia and neuromuscular disorders was completed, as was the first phase of the study of the use of the CK-BB assay in prostatic cancer. Preliminary results indicate that CK-BB is a new tumor marker for prostatic carcinoma and may have value in the early diagnosis of the disease. Work continues on the use and improvement of the serum CK-BB RIA in myocardial infarction, cardiac surgery, prostatic and other cancers. The use of CK-BB as a tumor marker for prostatic cancer appears very promising.

An evaluation of factors which interfere with the determination of uric acid was begun when discrepant values were noted in a patient with Burkitt's lymphoma who was treated with chemotherapy while on high doses of allopurinol. The study showed that high serum concentrations of xanthine act as a competitive inhibitor for the enzyme uricase and give a falsely low estimate for serum uric acid concentration when determined by this uricase method. The elevated xanthine concentration does not affect the phosphotungstate method.

A study on drug interference with the VMA determination was begun. Thus far, the results have shown that patients taking the drug L-dopa have a false elevation of urine VMA which increases on dilution of the samples. Studies are in progress to define the drug metabolite responsible for the interference with the VMA assay.

The interference of bromide in the serum with the determination of serum chloride by ion specific electrode and the thiocynate method was studied. Using an ion specific electrode for chloride, each milliequivalent of bromide was determined at 8 to 10 mEq of chloride. With the thiocynate method on the SMAC, each milliequivalent of bromide was determined as 2 mEq of chloride.

Using a sensitive electrophoretic procedure for lipoprotein analysis, patients with various abnormalities are being phenotyped. Extra lipoproteins and missing lipoproteins have been demonstrated.

In anticipation of expanded toxicology and trace metal analysis services, studies have begun on the proper methods and materials for collecting and storing specimens for heavy metal analysis.

A study of the sources of long-term variation in results for commercial radioimmunoassay kits was completed. We found considerable unexpected kit-to-kit variation in results for the $T_3$ and TSH assays. This is probably inherent in the nature of certain RIA procedures and must be anticipated in setting quality control criteria and reference ranges.

A study of lipoprotein patterns and ascorbic acid concentrations in patients on chronic hemodialysis was completed. Dietary supplementation of ascorbic acid did not modify lipoprotein patterns.

However, 95% of the patient population had a double pre-beta band whereas only 35% of the age and sex match control population had a similar finding. This was a significant difference and indicates a prevalent risk factor for accelerated atherosclerosis among the patient population.

A new assay system using a nephelometer was developed for the limulus test. Prior to the development of this system, the endpoint for the limulus assay had been gelation of lysate in a test tube. By using a carrousel for test tubes attached to a nephelometer, the rate of the interaction of the endotoxin with lysate could be monitored at 5 minute intervals. The variables of lysate concentration, heat for the reaction, and ionic strength were optimized for the assay. This instrument now permits the quantification of endotoxin to a concentration of 25 picrograms/ml in aqueous solution.

The Hematology Service has continued in major investigations of blood coagulation, morphology and erythrocytes. Studies have continued of the aging aspects of platelets by investigating specific platelet subcellular organelles such as lyzosomes, dense bodies, and mitochondria. It appears that the serotonin content and the number of dense bodies decreased with aging due to release of the storage sites. These techniques are being applied to specific platelet disorders.

Investigations into the isolation and function of the protein called cold insoluble globulin (CIg) are continuing. Studies have been performed on the purification of this protein and have looked at the effect of a variety of proteclytic enzymes on the fragmentation of CIg. These studies may be useful in determining molecular structure and provide a tool for determining which parts of the molecule of CIg are involved in this biological function.

Investigations are continuing of binding of factor VIII/von Willebrand factor protein to platelets which demonstrate the importance of the carbohydrate content in this binding.

Studies are continuing in determining the role of the factor VIII/von Willebrand factor protein in and on normal platelets. The studies include localization of the von Willebrand factor protein on platelets by specific antibody and localization of the coagulant portion of the factor VIII/von Willebrand factor protein by a second specific antibody. After immunofluorescent techniques demonstrate the presence or absence of these proteins, attempts will be made to see what their functional significance is in the interrelationships between platelets and the antibiotic ristocetin.

A study undertaken with the Medical Neurology Branch, NINCDS, and the Pediatric Oncology Branch, NCI, to determine the effect of plasmapheresis and plasma exchange by automated procedures on coagulation studies has been completed. The studies indicate that at the end of plasmapheresis, the patient tends to be anticoagulated and have a significant reduction in all coagulation proteins as well as inhibitors to coagulation (antithrombin III). Although we found no individual to have a clinical bleeding diathesis, subsequent studies of at least one patient in our institution revealed clinical bleeding after plasma exchange with albumin or plasminate. These studies are important in determining the side effects of plasmapheresis in hemostatically compromised individuals.

Studies on thrombin activation of factor VIII are continuing. The investigation has characterized the interaction of the factor VIII complex with thrombin. Studies have indicated that there is product inhibition of the reaction of thrombin with factor VIII. These studies will be important in our understanding of the defects in hemophilia and von Willebrand's disease.

Studies are continuing in cooperation with the NCI and the USUHS on the determination of terminal deoxynucleotidyl transferase (Tdt) as a marker for lymphoid malignancies. These studies are useful in determining small numbers of cells in the peripheral blood, bone marrow or body fluids which may have Tdt positivity and may indicate that there are a small percentage of malignant cells present. These studies are continuing to judge the significance of the immunofluorescent test for Tdt.

A study was undertaken at the NIH to look at the value of the hydroperoxidase stain for phi bodies in differentiating acute non-lymphocytic leukemia from acute lymphocytic leukemia. This specific stain was not of significant value to add any additional diagnostic information to the diagnosis of the leukemic state.

Studies are underway investigating the platelet membrane potential changes. Fluorescinated cyanine dyes when localized in biological membranes fluoresce in response to a transmembrane potential change. These studies have been applied to human platelets to determine the possibility of using this technique to assess normal platelet function. This work is being done in conjunction with the LCI, NIAID.

Studies are continuing in a cooperative venture with the NIAID in the study of the hypereosinophilic syndrome. Results of this study revealed a clinical and hematologic staging classification which appears to be able to separate those individuals who have a benign form of the disease from those who have a more myeloproliferative form of the disease. Application of this staging for both clinical and hematologic aspects of the disease clearly delineate at least four specific groups. This type of staging may be very beneficial in the choice of therapeutic regimens for patients at this institution as well as other institutions.

A study is in progress on the reduction of hemolysis in patients with impaired intracellular reductive activity, primarily patients with G6PD deficiency with a response to high doses of vitamin E. Preliminary examination of the data revealed that vitamin E appears to be useful in raising hemoglobin levels, reducing the reticulocyte counts, and prolonging red cell survival significantly in individuals treated with vitamin E compared to those not treated. Long-term studies are underway to see if the chronic hemolysis will continue to respond to vitamin E and if the number of hemolytic crises will be reduced with vitamin E therapy.

Studies in cooperation with the NHLBI and the Clinical Center Blood Bank on the use of young red blood cells for transfusion support in thalassemia are underway. Utilizing commercial cell separators which have been adapted to separate young red blood cells from older red blood cells as determined by age dependent enzyme assays and reticulocyte counts have been completed. The preliminary studies revealed that units containing 30 g of hemoglobin having a mean red cell age of 20 days compared to 60 days for whole blood have been isolated. Transfusion of these units into a patient with thalassemia revealed by radiochromium increased red cell survival. Only one patient thus far has been started in the study; other patients are awaiting entry.

Studies on the effect of low molecular weight factor VIII/von Willebrand factor on binding to the platelet surface and the clumping of platelets have been initiated. These studies reveal that binding of the small molecular weight von Willebrand factor proteins to the platelet surface is comparable to the large molecule weight species; however, these species do not support agglutination or aggregation of platelets. These studies may be of significance in 1) understanding the mechanism of the von Willebrand factor action with platelets and 2) as a form of protection against platelet-endothelial or platelet-platelet interaction which may be important in the genesis of atherosclerosis.

The cooperative venture has continued in the FAB group on the classification of leukemia and the clinical correlation with the morphologic subtypes with patient survival and ease of induction of first remission. A meeting was held again this year and a publication is forthcoming from this meeting.

In the Laboratory Computer Service, studies of the long-term analytic variation in clinical pathology tests have been carried out using results from patients, normal volunteers, and quality control specimens. The results of these studies are used by NIH clinical researchers whose projects involve laboratory data collected over several years. In addition, they are used by Clinical Pathology to identify sources of variation in analytical methods.

An evaluation of lot-to-lot variation in results obtained with three commercial radioimmunoassay kits has been carried out in collaboration with the Clinical Chemistry Service.

An ongoing collaborative study with the Microbiology Service utilizes a PDP-11 computer to detect bacterial growth in blood culture bottles by monitoring changes in electrical impedance.

An extensive computer analysis of Staphylococcus aureus phage typing patterns has been carried out in the Microbiology Service with the cooperation of the Laboratory Computer Service.

An extensive evaluation of a variety of methods for the determination of serum gentamicin was undertaken. This study evaluated the accuracy, cost, and ease of performance of each method. As a result of this study, a new method for determining gentamicin and other aminoglycoside antibiotics will shortly be implemented.

The studies on the Differential III, a laser light scattering detection instrument, have continued. A new computer algorithm has enabled us to start evaluating large numbers of organisms for rapid determination of antibiotic sensitivity and synergy studies.

Studies are continuing on the observation that bacteria will adhere to membranes with pore sizes much larger than the bacteria. It has been possible to elute these bacteria with the nonionic detergent, Tween 20.

A number of electrical, computer, and electrode problems have hindered work on the automated detection of bacteria in blood using impedance measuring techniques. At present, most of the electrical instability seems to have been solved, but a search continues for better electrode materials.

Studies on the distribution of an unnamed, but very antibiotic resistant, Corynebacterium species were completed. This organism was first noted in our patient population a few years ago, but a detailed study of its epidemiology was needed. It was found that it had a greatly increased pathogenicity in patients who were immunosuppressed and had hematologic as opposed to other malignancies.

The definitive speciation of alpha and nonhemalytic streptococci which were associated with human disease has been completed and the results are being readied for publication.

A study which correlated the determination of penicillinase producing activity of Staphylococcus aureus and S. epidermidis by using MIC values, penicillin zone edge characteristics and an acidometric determination of penicillinase was done. It was found that using the characteristics of the zone edge itself was a very reliable and simple indicator of penicillinase activity.

An ongoing study is being performed to corroborate the usefulness of Gram smear interpretation of throat cultures in predicting the presence of Group A beta hemolytic streptococci.

An evaluation of the feasibility of preparing biochemical tests in a microtiter plate using the MIC 2000, an automated dispensing instrument, has been initiated. This technique, if it produces results comparable to our present method, will provide the ability to test large numbers of bacteria at low cost.

### C. Training

Four first year residents entered the Clinical Pathology Department residency training program. They joined three second year residents in the program. Each rotation of the first year residency training program was evaluated by the residents using an evaluation sheet developed by the Office of the Chief. All comments and evaluations were transmitted to the Chiefs of the Services. This resulted in extending the length of the Chemistry rotation to 14 weeks and revising the rotation schedule and content for each Service.

The senior staff and the residents continued weekly Clinical Pathology Rounds in which interesting patients, laboratory problems, and original research were presented and discussed. These rounds are approved by the American Medical Association for Category I Continuing Medical Education credit.

The second year residents, while on the Resident-Consultant rotation, chose the following management-laboratory problems to evaluate: the need for toxicology analyses within the Clinical Center and the efficient use of blood products.

The Chemistry Service began a new series of lectures for continuing education for the medical technologists, based on case presentations. This series was approved for PACE and ACCENT credit.

The senior staff of the Chemistry Service began a bi-weekly research conference. Presentations were made by the senior staff to acquaint the Service with their research projects and obtain peer review.

In the Hematology Service training for new technologist has been improved by the use of a hematology procedures check list which gives a more structured approach to the training of new technologists. This list contains the basic items necessary for each work station and the new employee or supervisor of each section initial the items when completed to their mutual satisfaction. This insures proper and complete training of every technologist and technician who enters the Hematology Service.

Several members of the Hematology Service have participated in the review courses for Pediatric Hemato-Oncology course as well as adult oncology course. Lectures have been given concerning morphology, coagulation, and general areas of hematologic malignancies.

The Hematology Service continued to coordinate the Hematology-Oncology Clinical Elective and has continued its major role in the direction and teaching of this elective. Eleven medical students took their rotations in the Hematology Service from September 1977 through May 1978. Each student had a senior staff advisor who supervised all consultations by these students, who insured that the students were able to perform bone marrow aspirations and biopsies, and also assisted them in interpretation of peripheral blood smears and bone marrow material.

The senior staff, residents, and medical students of the Hematology Service met at least twice weekly to have rounds related to patients with hematologic problems. Patient-care and laboratory problems were presented at these rounds and discussed.

During the summer, three part-time employees have been directed in the area of hematologic research by individual advisors who have formulated research projects for these employees to perform during their time in the Hematology Service.

The Laboratory Computer Service conducted a three-week training course on medical computing for the residents. In addition, personnel from other Services were trained to use the NIH computer facilities for data processing.

Three Infectious Disease Fellows from the Bethesda Naval Hospital and one from the Walter Reed Army Hospital each spent one month in the Microbiology Service learning diagnostic bacteriology.

The senior staff continued biweekly lectures on practical bacteriology for the Clinical Pathology residents and other interested individuals from the area.

Weekly conferences with the senior staff and medical technologists and microbiologists were continued to discuss clinical cases and changes in procedures.

## IV. FUTURE OBJECTIVES

The Office of the Chief will continue to evaluate the efficient utilization of personnel and capital expenditures. When the College of American Pathologists workload system has been completely implemented, the Office of the Chief will have an effective tool for evaluating the utilization of personnel within the Department, and also a comparison with comparable hospitals within the country. The Office of the Chief will attempt to carefully evaluate the purchase of equipment for the Department, attempting to balance the quality of service with reasonable fiscal goals. Careful planning will be required in the upcoming years for the move to the new laboratory in the Ambulatory Care Research Facility (ACRF). A committee under the Office of the Chief composed of senior staff and technical personnel from each Service will coordinate plans and develop strategies for a smooth transition to the new laboratory.

The Clinical Chemistry Service will maintain the highest standards of quality while simultaneously increasing efficiency and output, as well as expanding the services offered to Clinical Center patient-care personnel. Through research and development and the use of new technology as it enters the market place, we hope to increase the accuracy and specificity of our tests and to investigate the clinical applicability of new areas of testing.

Therapeutic drug monitoring and trace metal analysis/toxicology will receive particular emphasis in the near future. Work on immunological approaches to measuring specific markers of tissue pathology (such as the work on creatine kinase isoenzymes) will continue and be expanded to include other types of markers which may be even more specific and sensitive.

The Clinical Chemistry Service has plans to perform almost all assays that are currently done by contract by 1982. The space for the accomplishment of this goal will be available in the ACRF. Additional personnel resources will also be needed for this goal to be realized.

The Hematology Service will continue to evaluate the automated analytical system, the Coulter S Plus, and if it continues to prove to be as efficacious and efficient as preliminary results suggest, we will attempt to purchase a second system for all samples.

The Hematology Service will continue to try to introduce new tests through research to better understand structure-function relationships of coagulation factors, platelets, red cells, and to develop tests which are more sensitive or predictive for bleeding or thrombosis in Clinical Center patients. Likewise, studies are continuing in the use of cell markers in delineating small numbers of leukemic cells which may be useful in 1) planning research protocols and 2) diagnosing early relapse of leukemic states.

An important service aspect of the Hematology Service will be to improve and continue the present standard of training in clinical consultations. It is hoped that through these two endeavors we can improve the care of the patients in the Clinical Center. To that extent, we are, in part, reconstructing the residency program for the Clinical Pathology residents in an attempt to further increase their involvement in the care of patients in the Clinical Center.

In the Laboratory Computer Service interfaces will be developed to permit laboratory instruments used for STAT analyses to be operated on-line to the Honeywell computer system. Honeywell programs will be modified to enhance the collection of quality control and workload data. A new system will be implemented for providing cumulative summaries of laboratory results for Clinical Center patients. Studies of biological and long-term analytical variation in clinical laboratory measurements will be continued.

In the Microbiology Service, it is hoped that the studies on laser light scattering instruments will reach a level of development to permit antibiotic synergy studies to be performed more readily than can now be accomplished.

The antibiotic sensitivity data base of over 50,000 isolates is being organized to permit an evaluation of how useful this data is in the identification of bacteria. A preliminary test performed a few years ago was encouraging, but the large number of isolates we have now should enable us to determine whether such identification checking is feasible.

The evaluation of the impedance blood culture detection system will, we hope, be completed in the near future. The search for a better electrode material should permit a more stable reading of the electronic data and should provide more consistent evaluation of cultures.

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Zweig, M.H., Silverman, L.M., Dermer, G.B., and Van Steirteghem, A.C.: Serum creatine kinase isoenzyme BB as an indicator of active metastatic disease. *Clin. Chem.* 25: 1190-1191, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10001-05 CP |

PERIOD COVERED
October 1, 1978 to September 30, 1979

TITLE OF PROJECT (80 characters or less)
Analytical Methodology: Development and Interpretation Application

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: R. J. Elin, Chief, Clinical Chemistry Service CP CC

OTHERS: E. A. Robertson, Assistant Chief, Laboratory Computer Serv. CP C
M. H. Zweig, Asst. Chief, Clinical Chemistry Service CP CC
Sharon McClean, Chemist CP CC

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 8 | 3 | 5 |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER
☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Analytical methods in use in clinical laboratories have been evaluated. New methods and instrumentation have been studied and effects of drugs on test values determined. Continued work with automatic interpretation of effects of drugs has shown that is possible to assist physicians in understanding influence of drug therapy in changing laboratory test values.

PHS-6040
(Rev. 10-76)

Project No. Z01 CC 10001-05 CP
1. Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 to September 30, 1979

Project Title: Analytical Methodology: Development and Interpretative Application

Previous Serial Number: Z01-CL-10001-04-CP

Principal Investigator: Ronald J. Elin

Other Investigators: E. Arthur Robertson
Mark H. Zweig
Sharon McClean

Man Years:

| | |
|---|---|
| Total | 8 |
| Professional | 3 |
| Other | 5 |

## Project Description

Objectives

1. To upgrade the quality of clinical laboratory data within NIH and elsewhere.

2. To facilitate the correct interpretation of laboratory data.

Methods employed:

1. Reference methods have been developed against which other methods can be compared. These methods are well characterized with respect to accuracy, precision, sensitivity and specificity.

2. Data bases have been developed in files to list effects of drugs on laboratory tests, conversion factors from traditional to SI units, and centers where unusual clinical laboratory tests are performed throughout the country.

Major findings:

Deficiencies in analytical methods have been identified and alternative methods studied in depth. By appropriate selection of method it is possible to avoid erroneous answers due to nonspecificity of the procedures. Drugs have been added to serum to their therapeutic concentration and effects observed on many different procedures on several different analyzers.

Significance:

This work has upgraded the quality of some tests in this laboratory and has the potential for doing the same thing in other laboratories when the same methods are used. By alerting physicians to drugs as a possible cause of abnormal data it has been possible to explain the cause of the unusual values and to prevent extensive and unnecessary workups of patients.

Proposed course:

Continued development and evaluation of methods will be undertaken.

Publications:

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Rodbard, D. and McClean, S.W.: Automated computer analysis for enzyme-multiplied immunological techniques. Clin. Chem. 23, 112-115, 1977.

Young, D.S. and Panek, E.: Effects of drugs on the analytical procedure of a multitest analyzer in Drug interferences and drug measurement in Clinical Chemistry. Siest, G., and Young, D.S. eds. Karger, Basel, pp 10-20, 1976.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-10004-04 CP |

PERIOD COVERED
October 1, 1978 to September 30, 1979

TITLE OF PROJECT (80 characters or less)

Radioimmunoassay of creatine kinase isoenzymes

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Dr. Mark H. Zweig, Staff Physician and Asst. Chief, Clinical Chemistry Service, CP,CC

Dr. Sharon McClean, Chemist, CP,CC

COOPERATING UNITS (if any) Dr. Andre Van Steirteghem, Brussels, Belgium; Drs. Ronald Feld and David Witte, Univ. of Iowa; Dr. Bruce Adornato, NINCDS; Dr. Lawrence Silverman, Good Samaritan Hospital, Los Angeles

LAB/BRANCH
Clin Path Dept

SECTION
Clinical Chemistry

INSTITUTE AND LOCATION
CC, NIH, Bethesda

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 0.5 | 1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Previously we developed radioimmunoassays for the MM and BB isoenzymes of creatine kinase in human serum. Currently we are investigating the clinical usefulness of these assays by measuring isoenzyme levels in serum and cerebrospinal fluid from patients with schizophrenia, in the serum, pleural fluid and prostatic fluid of patients with neuromuscular diseases, prostatic and other cancers, myocardial injury, and in the serum of patients undergoing cardiac surgery. The assay for the BB isoenzyme seems particularly useful. Elevations in CK-BB occur in neuromuscular diseases, myocardial infarction, prostatic and several other cancers, as well as following cardiac surgery. The use of serum CK-BB as a tumor marker in patients with prostatic and other carcinomas appears particularly promising.

-6040
(Rev. 10-76)

Project No. Z01 CL 10004-04 CP
1. Clinical Pathology Dept.
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Radioimmunoassay of Creatine Kinase Isoenzymes

Previous Serial No.: Z01 CL 10004-03

Principal Investigator: Dr. Mark Zweig

Other Investigator: Dr. Sharon McClean

Cooperating Units: Dr. Andre Van Steirteghem, Vrije Universiteit, Brussels, Belgium; Drs. Ronald Feld and David Witte, Dept. of Pathology, University of Iowa; Dr. Bruce Adornato, NINCDS; Dr. Lawrence Silverman, Good Samaritan Hospital, Los Angeles

Man Years:
Total 1.5
Professional 0.5
Other 1.0

## Project Description

Objectives:

1. To apply previously developed RIA's for creatine kinase (CK) isoenzymes to the diagnosis and study of disease of tissues and organs containing CK.

2. To optimize and shorten the assay for CK-BB so that it is more practical for routine clinical laboratory use.

Methods Employed:

1. Serum, pleural fluid, prostatic fluid and CSF were obtained from patients with a variety of disorders.

2. Total CK activity and isoenzymes MM and BB were assayed in these specimens.

Major Findings:

Serum CK-BB is often elevated in patients with untreated carcinoma and in patients with carcinoma which is not responding to therapy. In patients with prostatic carcinoma, CK-BB was elevated in 89% of those with untreated disease (stages B,C,D) but 0% of those with treated disease. It thus appears to have potential as a tool for the diagnosis of prostatic carcinoma.

Proposed Course:

Studies of CK-BB in serum of patients with myocardial infarction and after cardiac surgery will continue, to better define the applications of the test in patient management. Examination of patients with cancer will continue to determine what role CK-BB has in the diagnosis and staging of various cancers.

Publications:

1. Zweig, Mark H., and Van Steirteghem, Andre C.: Immunochemical determination of enzymes as tissue markers. Specific applications to the isoenzymes of creatine kinase in human serum, in Clinical Immunochemistry. Chemical and Cellular Bases and Applications in Disease. Natelson et al., eds., AACC, Washington, D. C., 1978, pp 401-408.

2. Zweig, MH. and Van Steirteghem, A.C.: Increased CK-BB concentrations in serum following cardiac surgery. Clin. Chim. Acta 93, 29-33 (1979).

3. Van Steirteghem, A.C., Robertson, E.A. and Zweig, M.H.: Distribution of serum concentrations of creatine kinase MM and BB isoenzymes measured by radioimmunoassay. Clin Chim Acta 93, 25-28 (1979).

4. Silverman, L.M., Dermer, G.B., Zweig, M.H., Van Steirteghem, A.C., and Tokes, Z.A.: Creatine kinase BB: A new tumor - associated marker. Clin. Chem. (1979), in press.

5. Zweig, M.H. and Van Steirteghem, A.C.: Creatine isoenzyme BB increases in serum after cardiac surgery. Clin. Chem. 24, 1853 (1978).

6. Zweig, M.H., Silverman, L.M., Dermer, G.B., and Van Steirteghem, A.C.: Serum creatine kinase isoenzyme BB as an indicator of active matastatic disease. Clin Chem. 25, 1190 (1979).

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-10005-5-CP |

PERIOD COVERED
October 1, 1978 to September 30, 1979

TITLE OF PROJECT (80 characters or less)

Development of a Nephelometric Procedure for the Quantitation of Pyrogens.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

H. Harold Nishi, CC, CPD - Research Biochemist, Principal Investigator

Ronald J. Elin, M.D.

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, MD 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>1.30 | PROFESSIONAL:<br>.30 | OTHER:<br>1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords) Endotoxins of gram-negative bacteria were found to react with the lysate of L. polyphemus amebocytes to form fine precipitin-like particles in the presence of large quantities of pyrogen-free sterile water. Light scatter measurements during the formation of these particles indicated that the rate of formation to be a function of endotoxin concentration. A enphelometric procedure for the quantitation of pyrogens (endotoxins of gram-negative bacteria) with Limulus amebocyte lysate (LAL) was developed and optimized by studying the various parameters of the reaction. The finalized procedure was established as 200 µl of LAL reagent with 100 µl of an endotoxin solution (reference or unknown solution) diluted to 2 ml with pyrogen-free sterile water. The end-point of the analysis was chosen as that time (minutes) at which the light scattering capacity of the particles reached 10 light scatter units above its baseline value. Studies indicated that the end-point data obtained on different levels of endotoxin can be defined with a mathematical formula. The standard curve data plotted on semi-log graph paper was a straight line. Reproducibility studies showed that the method was capable of giving a precision of 13% when testing endotoxin at a level of 100 pg/ml. The procedure permitted the quantitation of endotoxin as low as 16 pg/ml.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10005-5 CP
1. Clinical Center, Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial Number: Z01 CL 10005-4 CP

Principal Investigator: H. Harold Nishi

Other Investigator: Ronald J. Elin, M.D.

Cooperating Units: Inside NIH

Man Years:

| | |
|---|---|
| Total: | 1.30 |
| Professional | .30 |
| Other | 1.0 |

## Project Description

### Objective

The object of this research project is to develop a sensitive assay procedure for the quantitation of pyrogens (endotoxins of gram-negative bacteria) using the lysate of amebocytes from *Limulus polyphemus*.

### Method Employed

Nephelometry is used to measure the rate of precipitin-like particle formation resulting from the reaction of specific protein(s) found in the lysate of *Limulus polyphemus* amebocytes with endotoxins from gram-negative bacteria.

### Major Findings

The formation of light scattering precipitin-like particles during the reaction between pyrogens (endotoxins of gram-negative bacteria) and lysate of amebocytes from *Limulus polyphemus* (limulus amebocytes lysate--LAL) in large quantities of water indicated a possible quantitation of endotoxins by nephelometry. Light scatter measurements indicated that the rate of formation of these particles to be a function of endotoxin concentration. On the basis of these findings a new hephelometric procedure for the assay of endotoxins was formulated. The new procedure requires 200 µl of LAL reagent with 100 µl of an endotoxin solution or a dilution thereof (reference or unknown sample), in 2 ml with pyrogen-free sterile water. The end-point of the analysis was chosen at that time at which the light scattering capacity of the particles reach 10 light scatter units (LSU) above its baseline value. The rate of reaction or the increase in light scatter of the endotoxin and the reagent was found to follow a mathematical model of Log $Y=mX + a$. The Y is the

Major Findings (continued)

concentration of endotoxin in the sample in pg/ml, X is the time in minutes when 10 LSU was reached, m is the slope, and a is the Y intercept. The new procedure was optimized by studying the various parameters of the reaction and tested for reproducibility. Our present procedure indicates that endotoxins in fluids can be quantitated in the range of 16 to 1000 pg/ml with a precision of 13 and 11% at 100 and 500 pg/ml, respectively.

Significance

Based on the aggregate of our experience and the knowledge gained from our studies, we have developed a nephelometric assay procedure for endotoxins using lysate of L. polyphemus amebocytes which provides a simple reliable system for the quantitation of endotoxin for diagnostic care of NIH patients.

Proposed Course

1. To publish paper describing the new nephelometric procedure - in progress.
2. To automate the nephelometric procedure for endotoxin quantitation.
3. To increase rate of analyses by using kinetic rate measurements of endotoxin and LAL reaction.

Honors and Awards

None

Publications

None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10006-03 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Use of Laser Light Scattering for Rapid Determination of Potential Antibiotic Susceptibility and Synergy

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service, Laboratory Computer Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.1 | 0.1 | 1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The Differential III laser light scattering instrument is being evaluated for its potential usefulness for rapidly determining antibiotic synergy as well as susceptibility.

Project No. Z01 CL 10006-03 CP
1. Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Use of Laser Light Scattering for Rapid Determination of Potential Antibiotic Susceptibility and Synergy

Previous Serial No.: Z01 CL 10006-02

Principal Investigator: Dr. James D. MacLowry
Other Investigator: None
Cooperating Units: None

Man Years: Total 1.1
Professional 0.1
Other 1.0

## Project Description

### Objectives:

Evaluation of a prototype light scattering instrument, the Differential III for its potential use in clinical microbiology.

### Methods Employed:

Antibiotic combinations are being evaluated with a novel laser light scattering instrument to detect changes in bacterial growth. An updated more rapid instrument is in the final phases of evaluation.

### Major Findings:

The laser light scattering technique is very sensitive to the presence of and shape of particles. It has been necessary to capture the output of the instrument for computer analysis to detect significant changes.

### Significance to Biomedical Research and the Program of the Institute:

If this instrument and method can be made to work in a consistent fashion, it is possible that there will be a number of applications in clinical microbiology which would be useful. Specifically the ability to rapidly assay serum bactericidal activity and antibiotic bacteriocidal activity would be very useful if they can be done in a reasonable time frame with minimal cost.

Proposed Course:

Evaluation will continue until instrument has been adequately evaluated.

Honors and Awards:

None

Publications:

None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10009-04 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Blastocystis hominis, Structure, and Physiology

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Charles H. Zierdt, Microbiologist, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.1 | 0.25 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Blastocystis hominis, a protozoan parasite of the human gastrointestinal tract and an organism implicated in the causation of human diarrhea, is being studied in terms of its morphology, physiology, and sensitivity to metronidazole, enterovioform and similar drugs. This sporozoan may contain hundreds of mitochondria, although it is a strict anaerobe. Whether these are anaerobic mitochondria, and their enzyme activity, if any, are subjects of the study.

Project No.: Z01 CL-10009-04 CP
1. Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Blastocystis hominis, Structure, and Physiology

Previous Serial No.: Z01 CL-10009-03

Principal Investigator: Dr. Charles H. Zierdt
Other Investigator: None

Man Years:
Total: 0.1
Professional: 0.25
Other: 0.75

## Project Description

### Objectives:

Continuing study of *Blastocystis hominis*, newly designated protozoan parasite of man. By Feulgen staining many nuclei have been characterized in single cells. By thick and thin progressive sectioning for transmission electron microscopy, we are characterizing all of the nuclei in a series of single cells, to determine their places in the cell, and position vis a vis other organelles.

### Methods Employed:

Study of diarrhea caused by *B. hominis*, and the ultrastructure, physiology and life cycle of this organism.

### Honors and Awards:

None

### Publications:

Phillips, B. P. and Zierdt, C. H.: *Blastocystis hominis*: Pathogenic Potential in Human Patients and in Gnotobiotes. *Experimental Parasitology*. *39*: 358-364, 1976.

Publications: (continued)

Zierdt, C. H. and Tan, H. K.: Ultrastructure and Light Microscope Appearance of Blastocystis hominis in a Patient with Enteric Disease. Z. Parasitenk. 50: 277-283, 1976.

Zierdt, C. H.: Blastocystis hominis, an intestinal protozoan parasite of man. The Public Health Lab. 36: 147-159, 1978.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10010-04 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Effect of Magnesium Deficiency on Erythrocyte Structure and Function

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Ronald J. Elin Chief, Clin. Path. Dept. | CP CC |
| OTHER: | Dr. Laurence Corash, Asst. Chief, Hematology Serv. | CP CC |

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>2 | PROFESSIONAL:<br>.05 | OTHER:<br>1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Magnesium deficiency in experimental animals produces an anemia and a shortened erythrocyte survival. Experimental animals with severe magnesium deficiency produce erythrocytes with normal magnesium content, enzyme concentrations and structure. However, once this erythrocyte is subjected to an environment deficient in mangesium (plasma) structural and biochemical abnormalities occur which lead to the shortened erythrocyte survival.

PHS-6040
(Rev. 10-76)

Project No. Z01 CC 10010-04 CP
1. Clinical Pathology Dept.
2. Hematology Service
3. Bethesda, Maryland

PHS-NIH

Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Effect of Magnesium Deficiency on Erythrocyte Structure and Function

Previous Serial Number: Z01 CL 10010-03 CP

Principal Investigator: Dr. Ronald J. Elin
Other Investigator: Dr. Laurence Corash

Man Years:
Total: 2
Professional: .05
Other: 1.0

## Project Description

### Objectives:

Define and characterize membrane abnormalities associated with deficiency of magensium. Determine the effect of magnesium deficiency on erythropoiesis.

### Methods Employed:

The erythrocyte specimen was prepared by freeze-fracture and etching. The etched surface was coated with carbon and platinum. The specimen was then studied using an electron microscope. Erythrocytes from magnesium-deficient rats were separated on the basis of age using a stractan gradient. The magnesium concentration and pyrophosphatase activity were determined for each population of erythrocytes using standard techniques.

### Major Findings:

The erythrocytes from magnesium-deficient rats develop membrane alterations in the form of a plaque. These plaques were present on erythrocyte ghosts prepared by osmotic lysis. The membrane plaques were unaltered by incubating the cells in normal concentrations of magnesium. Erythropoiesis in magnesium-deficient rats is normal since reticulocytes and very young erythrocytes have a normal magnesium content, and normal concentration of erythrocyte pyrophosphatase and have a normal membrane surface. More mature erythrocytes show a decreased magnesium content, decreased erythrocyte pyrophosphatase activity and the development of membrane abnormalities in the form of plaques. In addition, the examination of the bone marrow of these animals shows normal erythroid precursors and an increased myeloid component.

Significance to Biomedical Research and the Program of the Department:

This is the first membrane abnormality of erythrocytes in experimental animals that is related to an abnormality in mineral metabolism. Magnesium has been clearly established as an essential element for biochemical processes involving energy production. In this study, magnesium has been shown to be important for normal membrane structures. This is part of a series of studies by the Department to define factors which influence erythrocyte survival and function. The structural and biochemical abnormalities of erythrocytes in magnesium deficiency occur after the cell has entered the vascular space. Thus, the bone marrow is able to produce a normal cell but an environment deficient in magnesium produces erythrocyte abnormalities.

Proposed course:

This project will now be extended to study factors of erythropoiesis that enable the synthesis of a relatively normal cell in magnesium deficiency.

Honors and Awards: None

Publications:

Elin, R. J.: Erythrocyte survival in magnesium-deficient rats. Proc. Soc. Exp. Biol. Med. 142: 1159-1161, April 1973.

Elin, R. J.: The effect of magnesium deficiency in mice on serum immunoglobulin concentrations and antibody plaque-forming cells. Proc. Soc. Exp. Biol. Med. 148: 620-624, March 1975.

Elin, R. J., and Tan, H. K.: Erythrocyte membrane plaques from rats with magnesium deficiency. Blood. 49:657-663, April 1977.

Elin, R. J. and Alling, D. W.: Survival of normal and magnesium-deficient erythrocytes in rats: effect of magnesium-deficient diet vs. splenectomy. J. Lab. Clin. Med., 91: 666-672, 1978.

Elin, R. J. and Tan, H. K.: Formation of plaques on erythrocyte membranes from rats with magnesium deficiency. Blood. 49: 657, 1977.

Elin, R. J.: Role of magnesium in membranes; erythrocyte and platelet function and stability. In Cantin, M. (ed.): Proceedings of the Second International Symposium on Magnesium. Spectrum Publications, New York, 1979.

Elin, R. J. and Tan, H. K.: Formation of plaques on erythrocyte membranes from rats with magnesium deficiency. In Cantin, M. (ed.): Proceedings of the Second International Symposium on Magnesium. Spectrum Publications, New York. 1979.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
**NOTICE OF**
**INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 CL 10012-11 CP

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Investigation of Hemorrhagic and Thrombotic Disorders in Man

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | |
|---|---|
| PI: Dr. Harvey R. Gralnick | Chief, Hematology Service CP CC |

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Dept., Clinical Center

SECTION

Hematology Service

INSTITUTE AND LOCATION

CP, CC, NIH, Bethesda, Maryland 20014

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 10.0 | 5.0 | 5.0 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☒ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Investigation of congenital and acquired hemorrhagic and thrombotic disorders in man to elucidate the clinical entities and to investigate the molecular basis for the defects. This has involved purification of coagulation proteins, immunologic investigation of coagulation proteins and inhibitors, and defining the role of these proteins in normal hemostasis and abnormal hemostasis.

Project No. Z01 CL 10012-11 CP

PHS-NIH
Individual Project Report

Project Title: Investigation of Hemorrhagic and Thrombotic Disorders in Man

Previous Serial Number: Z01 CL 10012-10

Principal Investigator: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total: | 10.0 |
| Professional: | 5.0 |
| Other: | 5.0 |

## Project Description

### Objectives:

Define and characterize normal and abnormal coagulation proteins, inhibitors, and cofactors associated with clinical disorders of hemostasis.

### Methods Employed:

Purification and isolation of various coagulation proteins, determination of functional defects, and molcular characterization of the defect. In addition multiple immunologic techniques are utilized for elucidation of abnormal proteins.

### Major Findings:

Three families with congenital dysfibrinogenemia have been fully described and elucidated. These families have defects in the conversion of fibrinogen to fibrin which interferes with normal hemostasis in two of the three families. The abnormalities vary in each family and in some families have been related to the release of fibrinopeptides and in others to polymerization of fibrin monomers. Studies of the pathological aspects of fibrinogen have indicated the importance of fibrinogen in maintenance of normal hemostasis. In particular, defects were observed in immunologic techniques, clotting techniques, and in the ability of fibrinogen to cross-link. In one family, the abnormal fibrinogen also had a markedly shortened intravascular survival.

Significance to Biomedical Research and the Program of the Department;

These studies elucidate some of the molecular defects associated with abnormal hemostasis and thrombosis and have allowed a greater understanding of the pathophysiology of blood coagulation. Not only have individual patients benefited from the elucidation of these defects in proper therapy but our greater understanding of blood coagulation in general has developed. This is part of a series of studies by this service to define the factors associated with hemorrhage and thrombosis in man.

Proposed Course:

This project will be extended to study other coagulation states and thrombotic states.

Honors and Awards:

None

Publications:

1. Gralnick, H., Abrell, E., and Bagley, J.: Heparin Treatment for Hemorrhagic Diathesis of Acute Promyelocytic Leukemia. Am. J. Med. 52: 167, 1972.

2. Gralnick, H., Givelber, H., Shainoff, J., and Finlayson, J.: Fibrinogen Bethesda: A Congenital Dysfibrinogenemia with Impaired Fibrinopeptide Release. J. Clin. Invest. 50: 1819, 1971.

3. Gralnick, H. and Abrell, E.: Studies of the Procoagulant and Fibrinolytic Activity of Promyelocytes in Acute Promyelocytic Leukemia. Brit. J. Haematol. 24: 89, 1973.

4. Gralnick, H. and Finlayson, J.: Congenital Dysfibrinogenemias. Ann. Int. Med. 77: 471, 1972.

5. Gralnick, H., Marchesi, S. and Givelber, H.: Intravascular Coagulation in Acute Leukemia. Blood 40: 709, 1972.

6. Gralnick, H., Givelber, H., and Finlayson, J.: A New Congenital Abnormality of Fibrinogen: Fibrinogen Bethesda II. Thromb. Diath. Haemorrh. 29: 562, 1973.

7. Gralnick, H. and Tan, H.: Acute Promyelocytic Leukemia: A Model for Understanding the Role of the Malignant Cell in Hemostasis. Hum. Pathol. 5: 661, 1974.

8. Frantantoni, J., Pollet, R., and Gralnick, H.: Heparin-induced Thrombocytopenia: Confirmation of Diagnosis with In Vitro Methods. Blood 45: 395, 1975.

9. Gralnick, H. and Sultan, C.: Acute Promyelocytic Leukemia: Haemorrhagic Manifestation and Morphologic Criteria. Brit. J. Haematol. 29: 273, 1975.

10. Greipp, P. and Gralnick, H.: Platelet to Leukocyte Adherence Phenomena Associated with Thrombocytopenia. Blood 47: 513, 1976.

11. Hoover, Jr., H. C., Ketcham, A. S., Millar, R. C., and Gralnick, H. R.: Osteosarcoma: Improved Survival with Anticoagulation and Amputation. Cancer, In press.

12. Horvath, A. and Gralnick, H. R.: The $^{125}$I Fibrinogen Euglobulin Lysis Test. Am. J. Clin. Path., In Press.

13. Spellman, Jr., G. G., Macoviak, J. A., and Gralnick, H. R.: Comparison of Polymerization of Ancrod and Thrombin Monomers. Blood 50: 619, 1977.

14. Gralnick, H. R.: Intravascular Coagulation. 1. Differential Diagnosis and Conditioning Mechanisms, and 2. Underlying Conditions and Therapy. Postgraduate Medicine 62: 68, 1977.

15. Gralnick, H. R., Givelber, H., and Abrams, E.: Dysfibrinogenemia Associated with Hepatoma: A Carbohydrate Abnormality. N. Engl. J. Med. In press.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10013-11 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Chemical and Structural Studies on the Human Factor VIII/von Willebrand Factor Protein

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Harvey R. Gralnick, M.D. Chief, Hematology Service CP CC

COOPERATING UNITS (if any)

Barry S. Coller, M.D., Div. of Hematology, School of Medicine, State Univ. of NY at Stony Brook, Stony Brook, N.Y.

Yvette Sultan, M.D., Dept. of Hematology, Hopital Saint-Louis, Paris, France

LAB/BRANCH

Clinical Pathology Dept., Clinical Center

SECTION

Hematology Service

INSTITUTE AND LOCATION

CP, CC, NIH, Bethesda, Maryland 20014

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 11.0 | 5.5 | 5.5 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

X (a1) MINORS (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The long-range purpose of this project is to initially study the immunologic aspects of the factor VIII/von Willebrand factor protein and then to study the biochemistry and structure of this protein in man. The topics of present interest are: (1) the defect of the factor VIII/von Willebrand factor protein in hemophilia A, (2) the defect of the factor VIII/von Willebrand factor protein in von Willebrand's disease, (3) the importance of carbohydrate content in biological functions, (4) the relationship of carbohydrate content to atherosclerosis, (5) the mechanism of thrombin activation, and (6) biochemical characterization of the biologically active sites of the factor VIII/von Willebrand factor protein.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10013-11 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Chemical and Structural Studies on the Human Factor VIII/von Willebrand Factor Protein

Previous Serial Number: Z01 CL 10013-11 CP

Principal Investigator: Dr. Harvey R. Gralnick

Other Investigators: Dr. Barry S. Coller
Dr. Yvette Sultan

Man years:

Total: 11.0
Professional: 5.5
Other: 5.5

## Project Description

Objectives:

Define and characterize the normal factor VIII/von Willebrand factor protein, to elucidate the defects of the protein in hemophilia and von Willebrand's disease and then to ascertain its role in atherosclerosis.

Methods Employed:

This has been accomplished by limited alpha chymotrypsin digestion of cryoprecipitate or other concentrates of factor VIII followed by gel chromatography on Sepharose 4B.

Major Findings:

Individuals with hemophilia A have a protein identical to normal in all respects except that it lacks clot-promoting activity while in von Willebrand's disease it has been found that the protein is quite heterogeneous. In some patients there is a complete absence of the protein with all its associated biological functions (quantitative defect) while in other patients there is a qualitative defect where the protein is present in normal amounts; however, it is deficient in biological activity. A major finding has been that the carbohydrate moiety of the factor VIII/von Willebrand factor protein is most important in its interaction with the platelets and vessel wall and may play an important role in the maintenance of normal hemostasis and propagation of atherosclerosis.

## Significance to Biomedical Research and the Program of the Department:

These studies further our long-term project of investigating hemorrhagic and thrombotic clinical disorders. The finding of the importance of carbohydrate in the interaction of platelets with vessel wall or with each other may not only be of major significance in the understanding of von Willibrand's disease but may be equally important in understanding the propagation of atherosclerosis.

## Proposed Course:

This project will be continued in its present phase with greater emphasis placed on the contribution of carbohydrates to platelet/platelet and platelet/vessel wall interaction. In addition, studies are underway to localize the sites on the factor VIII/von Willebrand factor protein which are involved in these interactions. Modification of these sites will be attempted in an effort to reproduce *in vitro* a von Willebrand's disease-like state.

## Honors and Awards:

1976 Fight for Sight Award for "von Willebrand Factor and Effect on Platelet Aggregation of Plasma from Diabetics with Retinopathy." Association for Research in Vision and Ophthalmology, Inc.

## Publications:

1. Gralnick, H., Abrell, E., and Bagley, J.: Immunologic Studies of Factor VIII (Antihemophiliac Globulin) in Hemophilia A. *Nature* 230: 9, 1971.
2. Marchesi, S., Shulman, N., and Gralnick, H.: Studies on the Purification and Characterization of Human Factor VIII. *J. Clin. Invest.* 51: 2151, 1972.
3. Gralnick, H., Coller, B., and Marchesi, S.: Immunological Studies of Factor VIII in Haemophilia and von Willebrand's Disease. *Nature New Biology* 244: 281, 1973.
4. Gralnick, H., Coller, B., and Marchesi, S.: Studies of the Human Factor VIII/von Willebrand Factor Portein. I. Comparison of the Protein Found in Normal, von Willebrand's Disease and Hemophilia A. *Thromb. Res.* 6: 93, 1975.
5. Gralnick H., Marchesi, S., and Coller, B.: Theoretical Approach to Molecular Biology of Factor VIII: Heterogeneity of the Molecule. *Ann. NY Acad. Sci.* 240: 378, 1975.

6. Coller, B., Hirschman, R., and Gralnick, H.: Studies of the Factor VIII/von Willebrand Factor Antigen on the Platelet Surface. Thromb. Res. 6: 469, 1975.

7. Gralnick, H. and Coller, B.: Studies on the Factor VIII/von Willebrand Factor Protein. II. Identification and Characterization of the von Willebrand Protein. Blood 46: 417, 1975.

8. Gralnick, H., Coller, B., and Sultan, Y.: Studies of the Human Factor VIII/von Willebrand Factor Protein. III. Qualitative Defect in von Willebrand's Disease. J. Clin. Invest. 56: 814, 1975.

9. Gralnick, H., Coller, B., and Sultan, Y.: Carbohydrate Deficiency of the Factor VIII/von Willebrand Factor Protein in von Willebrand's Disease Variants. Science 192: 56, 1976.

10. Gralnick, H. and Coller, B.: Molecular Defects in Hemophilia A and von Willebrand's Disease. Lancet, April 17, 1976.

11. Coller, B., Franza, Jr., B., and Gralnick, H.: The pH Dependence of Quantitative Ristocetin Aggregation: Theoretical and Practical Implications. A New Device for Maintenance of Platelet-Rich Plasma pH. Blood 47: 841, 1976.

12. Gralnick, H. R., Sultan, Y., and Coller, B. S.: von Willebrand's Disease Combined Qualitative and Quantitative Abnormalities. N. Engl. J. Med. 296: 1024, 1977.

13. Gralnick, H. R., Coller, B. S., Shulman, N. R., Andersen, J. C., and Hilgartner, M.: Factor VIII. Ann. Int. Med. 86: 598, 1977.

14. Coller, B. S. and Gralnick, H. R.: Studies on the Mechanism of Ristocetin-Induced Platelet Agglutination: Effects of Structural Modification of Ristocetin and Vancomycin. J. Clin. Invest. 60: 302, 1977.

15. Gralnick, H. R.: Factor VIII/von Willebrand Factor Protein: Galactose--A Cryptic Determinant of von Willebrand Factor Activity. J. Clin. Invest., In press.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10016-03 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Qualitative Improvement of Blood Transfusion Using Young Cell Cohorts

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Laurence Corash, M.D. | Assistant Chief | Hematology Service CP CC |
| Other: | H. Klein, M.D. | Assistant Chief | Blood Bank, CC |
| | A. Diesseroth, M.D. | Section Chief | Pediatric Oncology NCI |
| | A. Nienhuis, M.D. | Chief Clinical Hematology | NHLBI |

COOPERATING UNITS (if any)

S. Piomelli, Dept. of Pediatrics, New YORK University School of Medicine
New York, NY 10016

LAB/BRANCH

Clinical Pathology Department

SECTION

Hematology Service

INSTITUTE AND LOCATION

CP, CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.8 | 0.5 | 0.3 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purpose of this study is to demonstrate that Stractan separated yound red blood cells can be transfused into autologous non-human promate donors and that these cells have an improved survival compared to whole blood. Preliminary studies have shown that young red cells from rabbits can be isolated and transfused by this method. These cells demonstrate a markedly improved survival compared to unfractionated whole blood. The rhesus monkey model has been developed and demonstrates that young red cells can be isolated by this method and have improved post transfusion survival. A solid phase radioimmunoassy was developed to look for antigalactan antibodies in treated animals and in untreated normal human subjects of all ages. The eventual goal of this project will be to explore the use of this system for human transfusion, thus reducing the transfused iron load in patients with chronic anemias.

The study has been expanded to use presently available cell separates to prepare units for transfusion of young red blood cells. Estimated cell ages have been derived by use of age dependent enzymes and reticulocyte counts.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10016 - 03 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Qualitative Improvement of Blood Transfusion Using Young Cell Cohorts

Previous Serial Number: Z01 CL 00016-02

Principal Investigator: Dr. Laurence Corash

Other Investigators:
Dr. H. Klein
Dr. A. Deisseroth
Dr. A. Nienhuis

Man Years:

| | |
|---|---|
| Total: | 0.8 |
| Professional: | 0.5 |
| Other: | 0.3 |

## Project Description

### Objectives:

1. Development of a rhesus monkey model to examine the survival of Stractan separated age dependent red cell cohorts.

2. To determine if naturally occurring arabino-galactan antibodies exist in humans and rhesus monkeys and to determine if they develop in animals after exposure to arabino-galactan treated cells.

3. To modify existing technology, IBM and Aminco cell separators, to prepare young red cells for transfusion.

### Methods:

Age dependent red cell cohorts were obtained with arabino-galactan density gradients. Red cell life span is measured with radiochromium or radioactive cyanate. Radioimmunoassay using an iodinated myeloma protein with anti-arabino-galactan specificity. Young red cells were obtained by use of continuous flow cell separator devices.

## Major Findings:

Young red cells from rabbits have an improved survival compared to old red cells when transfused in autologous donors. Experiments in the rhesus model were similar. Young red cells were prepared and chromium 51 red cell survivals in beta thalassemia patients confirm a greatly improved red cell survival.

## Significance:

This technology may provide a means for qualitatively improved red cell transfusion, thus limiting iron overload in patients with chronic transfusion requirements. Adaptation of currently available cell separators to this basic methodology makes rapid inception of this approach readily feasible. A current transfusion program has been started by the author.

## Awards and Honors:

NIH Grant HL-19946-1. "Reduction of Iron Overload in Thalassemia"

## Publications:

1. Corash, L., Piomelli, S., Seaman, C., Comisa, C.: High Resolution Separation of Blood Cell Types by Density Gradient Centrifugation. Blood 42: 1006, 1973.

2. Corash, L., Piomelli, S., Chen, H., Seaman, C., Gross, E.: Separation of Erythrocytes According to Age on a Simplified Density Gradient. J. Lab. Clin. Med. 84: 147-151, 1974.

3. Corash, L., Seaman, C., Comisa, C., Reibman, J. R., Piomelli, S.: Separation of RBC's with Improved Survival from Normal Blood. Ped. Res. 8: 399, 1974.

4. Corash, L., Seaman, C., Reibman, J., Tytun, A, Piomelli, S.: Qualitatively Improved Blood Cell Transfusion. A New Approach to Therapy of Chronic Anemias. 16th Meeting, Int. Soc. Hem., Kyoto, Japan, 1976.

5. Piomelli, S., Seaman, C., Reibman, J., Tytun, A., Graziano, J., Tabachnick, N., Corash, L.: Separation of Younger Red Cells with Improved "In Vivo" Survival: A New Approach to Chronic Transfusion Therapy. Proc. Natl. Acad. Sci. 75: 3474-3478, 1978

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10019-03 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Resistant Corynebacterium - Further Characterization and Identification of Normal Habitat.

**NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT**

PI: Dr. Vee J. Gill, Supervisory Microbiologist, Microbiology Service, CPD, CC.

OTHER: Dr. Frank G. Witebsky, Asst. Chief, Microbiology Service, CPD, CC.
Dr. Philip A. Pizzo, Pediatric Oncology Branch, Division of Cancer Treatment.

COOPERATING UNITS (if any)

Pediatric Oncolocy Branch, NCI

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.5 | 0.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

An antibiotic-resistant Corynebacterium sp. has been isolated with increasing frequency from severely immunosuppressed patients at the Clinical Center and now also at other Cancer hospitals. Isolates of this organism were collected and further characterized since this Corynebacterium seems to be an un-named species designated as group J/K with little information currently available as to its frequency and distribution. Screening cultures indicate that hospitalized patients may harbor the organism particularly on axillary and inguinal skin sites. Isolation is greater from males than females, and patients may frequently harbor the organism on admission to the N.I.H. hospital, indicating prior colonization. Colonization occurs in both cancer and non-cancer patients, but bacteremia has occurred exclusively in cancer patients, specifically in those with hematologic as opposed to solid neoplasms.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10019-03
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Resistant Corynebacterium - Further Characterization and Identification of Normal Habitat

Previous Serial No.: Z01 CL 10019-02

Principal Investigator: Dr. Vee J. Gill
Other Investigators: Dr. Frank G. Witebsky
Dr. Philip A. Pizzo
Cooperating Units: Pediatric Oncology Branch, NCI

Man Years: Total: 1.0
Professional: 0.5
Other: 0.5

## Project Description

### Objectives:

Further characterize with respect to biochemical characteristics and antibiotic sensitivity patterns, a resistant corynebacterium species. Determine the normal habitat of this organism. Determine the types of patients and predisposing characteristics to colonization and infection with this organism.

### Methods Employed:

Organisms isolated from a variety of clinical specimens and found to be this antibiotic-resistant Corynebacterium species were evaluated for their biochemical characteristics and specific antimicrobial sensitivity pattern by in vitro testing procedures. A culture medium selective for this organism has been devised to aid in isolation, thus allowing us to screen numerous specimens as well as do survey cultures on normal volunteers and patients to define the organism's normal habitat. Information on all patients from which the organism was isolated was compiled.

## Major Findings

These antibiotic-resistant Corynebacteria are biochemically homogeneous in their reactions, indicating that they probably represent a single species. There is some variability in their antibiotic resistance patterns mainly with tetracycline, erythromycin and gentamicin. They are consistently sensitive to vancomycin which is used for treatment when necessary. The organism probably resides as part of the skin flora of hospital patients particularly in the acilla and groin. Routine isolates were predominantly from wounds, abscesses and lesions, and predominantly from male patients. Although colonization rates on two wards were approximately 30% (cancer and non-cancer patients), bacteremia only occurred in cancer patients.

## Significance to Biomedical Research and the Program of the Institute:

This organism can be a significant pathogen, particularly in compromised hosts. Further characterization of the species and its ecology is important for understanding the pathogenesis of and selecting appropriate treatment for disease caused by this organism. The project is now completed and the information will be submitted for publication.

## Presentations:

"Antibiotic-Resistant Corynebacterium on Oncology Wards" in Symposium on Advances in the Recognition of Human Pathogens. A.S.M. Annual Meeting, Los Angeles, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10022-04 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Detection of Bacteremia Using an Electrical Impedance Detection System

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | |
|---|---|
| PI: | Dr. Charles H. Zierdt, Microbiologist, Microbiology Service, CPD, CC |
| OTHER: | Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC |
| | Mr. Edward Hall, Engineer, B.E.I.B. |
| | Dr. E. Arthur Robertson, Asst. Chief, Laboratory Computer Service |
| | Mr. Robert Harshman, Computer Programmer, Laboratory Computer Service |

COOPERATING UNITS (if any)

Biomedical Engineering and Instrumentation Branch, DRS, NIH

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service, Laboratory Computer Service, B.E.I.B.

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.25 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A prototype instrument has been constructed and improved which allows the monitoring of blood cultures with an electrical impedance detector.

Various problems of unreliability in the impedance detection electronics have plagued this study for a full year. Two of the problems were heat in the 37°C incubator affecting components in the circuitry, and an inadequate power supply transformer. The impedance detection apparatus has been moved out of the incubator, and a larger component to supply power has been added.

Project No. Z01 CL-10022-04 CP
1. Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Detection of Bacteremia Using an Electrical Impedance Detection System

Previous Serial No.: Z01 CL-10022-03 CP

Principal Investigator: Dr. Charles H. Zierdt
Other Investigators: Dr. James D. MacLowry
Mr. Edward Hall
Dr. E. Arthur Robertson
Mr. Robert Harshman

Man Years:
Total: 1.0
Professional 0.25
Other: 0.75

## Project Description

Objectives:

An attempt is being made to more rapidly detect positive clinical blood cultures in an automated fashion.

Methods Employed:

A prototype impedance detector has been developed and connected to a dedicated computer in the laboratory. This represents a novel approach to detection of bacterial cultures by using a very minimum amount of human ntervention. The blood has been lysed and filtered before presentation o the detector to increase bacterial yield.

ajor Findings:

lood cultures are detected more rapidly and fewer colony forming units an be detected than by conventional methods.

ignificance to Biomedical Research and the Program of the Institute:

his methodology may enable a routine diagnostic laboratory to detect acteremia more rapidly than with conventional means.

## Proposed Course:

We will continue to evaluate patient specimens in parallel with our traditional method to confirm the initial observations with this method. We are searching for a better electrode material than the stainless steel that we presently use. Stainless steel corrodes somewhat under the conditions of use for impedance detection, where it is heated to red heat for reuse.

## Honors and Awards:

None

## Publications:

1. Zierdt, C. H., Kagan, R. L. and MacLowry, J. D.: Development of Lysis-Filtration Blood Culture Technique. J. Clin. Microbiol. 5: 46-50, 1977.
2. Kagan, R. L., Schuette, W. H., Zierdt, C. H. and MacLowry, J. D.: Rapid Automated Diagnosis of Bacteremia by Impedance Detection. J. Clin. Microbiol. 5: 51-57, 1977.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10025 03 CP |

PERIOD COVERED
October 1, 1978 to September 30, 1979

TITLE OF PROJECT (80 characters or less)

Clinical Laboratory Applications of Microcalorimetry

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Nadja N. Rehak, Ph.D.

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, MD 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.6 | 0.4 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A heat-conduction type batch microcalorimeter has been used for quantitative measurements of body fluid components. Measurements of chymotrypsin, pepsin, trypsin and lactate dehydrogenase were carried out using kinetic calorimetry. Measurement of total heat was used for quantitation of uric acid and total cholesterol. Differentiation of lactate dehydrogenase isoenzymes and free and esterfied cholesterol was accomplished. Studies are continuing on the calorimetric assays that employ antigen-antibody reactions.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10025-03 CP
1. Clinical Center, Clinical Path.
   Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 1979

Previous Serial Number: Z01 CL 10025-02 CP

Principal Investigator: N. N. Rehak, Ph.D.

Other Investigator: None

Cooperating Units: None

Man Years:

| | |
|---|---|
| Total: | 0.6 |
| Professional: | 0.4 |
| Other: | 0.2 |

## Project Description

### Objective

To determine the feasibility of calorimetry as a technique in clinical laboratory.

### Methods Employed

Calorimetric assays of body fluids components were compared against conventional routine methods used in clinical laboratory.

### Major Findings

Calorimetric technique can be used for quantitative measurements of both metabolites and enzymes in body fluids. The sensitivity and precision of the calorimetric measurements is comparable to the proposed reference methods and the routine clinical assays. The calorimetric method requires minimal sample manipulation and is prone to less interferences than the corresponding spectrophotometric methods. Calorimetry can be used for differentiation of two simultaneous or sequential reactions which enables simultaneous quantitation of two different body fluid components.

### Sifnificance

The accuracy and simplicity of calorimetric measurements indicate the possible application of this technique in the development of reference methods for Clinical Chemistry.

Proposed Course

The specificity of reaction, that is required for calorimetric measurements, can be achieved with the use of appropriate antibody. Preliminary calorimetric measurement of albumin-antialbumin reaction will be followed by more detailed thermochemical studies of the reaction. Calorimetric measurement of albumin will be compared with the nephelometric albumin determinations.

Publications

None

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CL 10027-02 CP

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Platelet Serotonin Metabolism

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Laurence Corash, M.D. | Assistant Chief, Hematology Ser. CP | CC |
| Other: | J. Costa, M.D. | Staff Physician | LCS,NIMH |

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department

SECTION

Hematology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 0.3 | PROFESSIONAL: 0.1 | OTHER: 0.2 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Serotonin is a vaso-active amine which is highly concentrated in the blood platelet. Release of serotonin in response to platelet activating stimuli may play a role in many pathologic states. The absence of platelet serotonin is associated with severe platelet dysfunction and a hemorrhagic diathesis. We have modified a sensitive assay to accurately measure platelet endogenous serotonin content in normal subjects and patients. Young, heavy platelets contain four times the serotonin of old, light platelets. Thus, platelet serotonin content may be a useful means to measure platelet turnover rates. Isolation of age dependent platelet cohorts permits the study of serotonin uptake, content and release in a varieyt of pathologic states.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10027-02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial Number: Z01 CL 10027 01
Project Title: Platelet Serotonin Metabolism

Principal Investigator: Dr. Laurence Corash

Other Investigators: Dr. J. Costa

Man Years:

| | |
|---|---|
| Total: | 0.3 |
| Professional: | 0.1 |
| Other: | 0.2 |

## Project Description

### Objectives:

1. Measurement of platelet endogenous serotonin content.

2. Quantification of serotonin storage sites and transport rates in age dependent platelet cohorts.

### Methods Employed:

Platelets were isolated by use of arabino-galactan gradients. Serotonin transport was measured by rapid uptake of radioactive serotonin and formaldehyde fixation. Serotonin content was measured by a specific double isotope dilution assay.

### Major Findings:

1. Serotonin storage sites, platelet dense bodies, are distributed in an age dependent fashion among platelets.

2. The rate of transport is equal in young and old platelets.

3. Young platelets contain four times the serotonin content of old platelets. This is due to a decreased number of storage sites.

### Significance:

Platelet serotonin is important for normal platelet function and may play a role in pathologic states that involve the platelet release reaction. The methodologies developed in this study serve to better understand these disorders.

Awards and Honors:

None

Publications:

1. Corash, L, Costa, J., Tan, H., Shafer, B., Fauci, A.S., Wolff, S.M.: 5-Hydroxytryptamine Metabolism, Alpha Granule Release and Life Span of Chediak-Higashi Syndrome Platelets. Clin. Res. 25: 337A, 1977.

2. Costa, J.L., Stark, H., Shafer, B., Corash, L., Smith, M.A., Murphy, D.L.: Maximal Packet Size for Serotonin in Storage Vesicles of Intact Human Platelets. Life Sciences 23:2193-2198, 1978.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10028-02 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Platelet Aging

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Laurence M. Corash | Assistant Chief, Hematology Service, CP, CC |
| Other: | Dr. Henry K. Tan | Palomar Memorial Hospital California |
| | Dr. Mark Perlow | Staff Fellow M SMRC |
| | Dr. Jon Costa | Staff Physician, Lab. of Neuropharmacology NIMH |
| | Dr. Dennis Murphy | Chief, Lab. of Neuropharmacology, NIMH |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.5 | 0.5 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Blood platelets have a finite life span in the peripheral circulation and under normal steady state conditions are removed by a discrete aging process. Earlier studies had suggested that there were structural, metabolic, and functional differences between young and old platelets. Existing methods to isolate platelets for study were inadequate. An efficient method to quantatively isolate pure blood platelets has been developed in this laboratory. Experiments have shown that there is a strong relationship between platelet density and platelet structure, metabolism and function. Use of a non-human primate model has shown that these density dependent characteristics do correlate with platelet age. Thus, it is now possible to isolate age dependent platelet cohorts and to measure age dependent parameters of pure whole blood platelets. These techniques provide a means to analyze mechanisms of platelet aging to estimate platelet turnover rates, and to isolate platelets of improved quality for potential use in therapeutic transfusion.

Project No. Z01 CL 10028 02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial Number: Z01 CL 10028 01 CP
Project Title: Platelet Aging

Principal Investigator: Dr. Laurence M. Corash

Other Investigators: Dr. Henry K. Tan
Dr. Mark Perlow
Dr. Jon Costa
Dr. Dennis Murphy

Man Years:

| | |
|---|---|
| Total: | 1.0 |
| Professional: | 0.5 |
| Other: | 0.5 |

## Project Description

### Objectives:

1. Isolation of pure whole blood platelets which are structurally and functionally intact.
2. Correlation of platelet density with structure, metabolism and function.
3. Development of a sub-human primate model to prove that platelet density is an age dependent parameter.
4. Evaluation of platelet size, serotonin content and glycolytic rate as a means to estimate platelet turnover rate in patients with various platelet disorders.
5. Measurement of biochemical activity associated with different subcellular organelles: mitochondria, lysosome and dense bodies.

### Methods Employed:

Platelets were isolated from whole blood and separated into density dependent cohorts by use of isosmolar arabino-galactan discontinuous gradients and ultra-centrifugation. Cell volume distribution was measured with an electronic particle counter equipped with a logarithmic amplifier and a small computer. Platelet ultrastructure was viewed with transmission electron microscopy. Platelet function was evaluated by aggregation to standard platelet stimulating agents. A sensitive double isotopic radioactive assay was adopted to measure endogenous serotonin content. The rhesus monkey model was developed to isolate density dependent platelet cohorts which were labelled and radiochromium and reinfused into donor animals to measure cohort life span.

Monoamine oxidase activity, beta glucuronidase activity, dense body content, serotonin content and transport rate as well as release were measured.

Major Findings:

1. Pure whole blood platelets in high yield can be isolated by this technique.
2. Traditional isolation methods are biased in favor of smaller, lighter platelets.
3. Platelets can be effectively isolated from plasma proteins and then be reconstituted to a functional state with autologous plasma.
4. There is a significant correlation between platelet density and cell volume, structure and organelle content.
5. A well defined range of platelet size distribution exists and was defined for a large population of normal subjects.
6. Simultaneous platelet size determination and standard radiochromium platelet survivals were performed in patients. There is a strong correlation between decreased platelet life span and increased platelet volume.
7. The rhesus monkey model has shown that heavy platelets have a longer survival than do light platelets. Introduction of a heavy platelet cohort label into the bottom of a gradient results in progressive migration of the label up through the gradient, thus clearly demonstrating that heavy platelets become light platelets.
8. Heavy platelets contain four times the serotonin content of light platelets, thus serving as a useful age dependent marker.
9. Although platelet mitochondria number does not vary with cell age, younger platelets consistently have higher monoamine oxidase activity. Young platelets contain more dense bodies than old platelets but serotonin packet size and releasability are equivalent.

Significance

Earlier techniques have not been able to efficiently isolate whole blood platelets. This method removes all plasma proteins from platelets which was not possible by earlier methods. For the first time age dependent platelet cohorts from a total whole blood platelet population can be isolated.

Subsequent study of these cell cohorts will permit evaluation of aging effect on platelets in disease. This method will also provide diagnostic information to discriminate diseases with increased platelet destruction from diseases with failure of platelet production. It will also facilitate studies to determine if platelet disorders are due to a qualitative protein defect or a quantitative protein defect. This study provides a new method to explore platelet aging.

Proposed Course:

The project is now being extended to apply the method to patients with platelet disorders. The animal model will be manipulated to perform in vivo experiments which cannot be performed in patients.

Honors and Awards:

None

Publications:

1. Corash, L., Gralnick, H.R.: High Yield Quantitative Isolation of Human Platelets from Whole Blood. Blood 44:919, 1974.
2. Corash, L., Tan, H., Gralnick, H.: Heterogeneity of Human Whole Blood Platelet Subpopulations. I. Relationship Between Buoyant Density, Cell Volume, and Ultrastructure. Blood 49:71-87, 1977.
3. Corash, L., Shafer, B., Weinberg, D., Steinfeld, M.B.: Platelet Sizing of Whole Blood Total Platelet Populations in Platelet Function Testing, Day, H.J., Holmsen, H., Zucker, M.D. (eds.). Dept. HEW Publication, NIH 78-1087, pp. 315-322 and pp. 773-737, 1976.
4. Andersen, J., Gralnick, H., Corash, L.: Partial Characterization of Platelet Associated Factor VIII. Circulation 54:II-115, 1976.
5. Corash, L., Costa, J., Tan, H., Shafer, B., Fauci, A.S., Wolff, S.M.: 5-Hydrozytryptamine Metabolism, Alpha Granule Release, and Life Span of Chediak-Higashi Syndrome Platelets. Clin. Res. 25:337A, 1977.
6. Norton, J.A., Shulman, N.R., Corash, L., Smith, R.L., Au, F., Rosenberg, S.A.: Severe Thrombocytopenia Following Intralesional BCG Therapy. Cancer 41:820-826, 1978.
7. Murphy, D.L., Costa, J.L., Shafer, B., Corash, L.: Monoamine Oxidase Activity in Different Density Gradient Fractions of Human Platelets. Psychopharmacology 59:193-197, 1978.

8. Goldstein, R.E., Corash, L., Capurro, N.L., Andersen, J.C., Epstein, S.E.: Decrease in Platelet Survival and Enhancement of Sympathetically Mediated Reflex Rises in Heart Rate After Abrupt Withdrawal of Propanolol. Clin. Res. 26:235A, 1978.

9. Corash, L., Costa, J.L., Shafer, B., Pettigrew, K., Murphy, D.: Platelet Organelle Content: Biochemical Activity and Relationship to Platelet Aging. Clin. Res. 26:345A, 1978.

10. Corash, L., Shafer, B., Perlow, M.: Platelet Heterogeneity: Relationship Between Buoyant Density and Cell Age. Clin. Res. 26:345A, 1978.

11. Corash, L., Shafer, B., Perlow, M.: Heterogeneity of Human Whole Blood Platelet Subpopulations. II. Use of a Sub-Human Primate Model to Analyze the Relationship Between Density and Platelet Age. Blood 52:726-734, 1978.

12. Tan, H.K., Harrison, M., Corash, L.: Demonstration of the Outer Surface of Freeze Etched Normal Human Platelets: Correlation with Buoyant Density. Br. J. Haematol. 40:289-298, 1978.

13. Costa, J.L., Stark, H., Shafer, B., Corash, L., Smith, M.A., Murphy, D.L.: Maximal Packet Size for Serotonin in Storage Vesicles of Intact Human Platelets. Life Sciences 23:2193-2198, 1978.

14. Corash, L.: Platelet Heterogeneity: Relationship Between Density and Age in The Blood Platelet in Transfusion. Jamieson, G., Greenwalt, T. (eds.), A.R. Liss, Inc., New York, 1978, pp. 79-82.

NUCLEAR MED.
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FABRIC CARE
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DIAG. RADIOL.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
**NOTICE OF**
**INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 CL 10029-02 CP

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Protective Effect of Vitamin E on Oxidative Related Hemolysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Joseph Schulman, M.D. | Chief, Medical Genetics Section | NICHD |
| | Laurence Corash, M.D. | Asst. Chief, Hematology Service, CP | CC |
| | Stephen Spielberg, M.D. | Asst. Prof., Dept. of Pharmacology<br>Johns Hopkins Medical School<br>Baltimore, Maryland | |
| | Lawrence Boxer, M.D. | Assoc. Prof., Dept. of Pediatrics<br>University of Indiana School of<br>Medicine, Indianapolis, Indiana | |

COOPERATING UNITS (if any)
Johns Hopkins University Medical School
University of Indiana School of Medicine

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 0.4 | PROFESSIONAL: 0.4 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☒ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients with chronic hemolysis due to defects in production of reduced glutathione or reduced nucleotides are being treated with large doses of vitamin E. It is postulated that vitamin E can act as a free radical scavenger and provide a partial protective effect against oxidative related hemolysis in this group of patients. Red cell survival pre- and post-therapy, as well as routine hematologic parameters and clinical course, are being monitored to evaluate the efficacy of this therapeutic approach. A large clinical trial of high dose vitamin E therapy has been completed in Greek Mediterranean type glucose-6-phosphate dehydrogenase deficient subjects.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10029-02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Protective Effect of Vitamin E on Oxidative Related Hemolysis
Previous Serial No.: None
Principal Investigator: Dr. Laurence M. Corash

Other Investigators: Dr. Joseph Schulman
Dr. Stephen Spielberg
Dr. Lawrence Boxer

Man Years:
Total: 0.4
Professional: 0.4
Other:

## Project Description

### Objectives:

To determine if oral high dose vitamin E therapy can increase red cell survival in patients with defects in reduced nucleotide or reduced glutathione production disorders.

### Methods Employed:

Routine hematologic studies are used to assess clinical status. Red cell survival studies are performed using autologous radiochromated red cells. Clinical status and red cell survival are measured before and after three months of therapy.

### Major Findings:

One patient with severe chronic hemolysis due to G6PD deficiency showed improvement with therapy. A second patient with glutathione synthetase deficiency was also improved with vitamin E therapy. Thirty-eight patients with G6PD deficiency of the Mediterranean type were entered into a cooperative study with this laboratory and Dr. C. Bartsocas, Athens, Greece. This study was completed and demonstrated a significant reduction in degree of chronic hemolysis with therapy.

### Significance:

Severe hemolysis due to oxidative stress occurs in patients with red cell deficiencies of reduced nucleotides or glutathione. These hemolytic crises may contribute to associated disorders or result in death. Eighty million people are affected by G6PD deficiency. High dose vitamin E therapy may offer a protective effect to these patients against oxidative stresses with subsequent hemolysis. The ultimate goal of this therapy will be to reduce both mortality and morbidity.

Proposed Course:

Studies in severely affected patients with chronic hemolysis will be extended. The Greek study in patients with episodic hemolysis will be completed and if warranted a large scale multicenter trial will be initiated.

Publications:

1. Spielberg, S.P., Garrick, M.D., Corash, L.M., Butler, J.D., Tietze, F., Rodgers, L., Schulman, J.: Biochemical Heterogeneity in Human Glutathione Synthetase Deficiency. J. Clin. Invest. 62:1417-1420, 1978.

2. Spielberg, S.P., Boxer, L.A., Corash, L.M., Schulman, J.D.: Improved Erythrocyte Survival with High Dose Vitamin E in Chronic Hemolyzing G6PD and Glutathione Synthetase Deficiencies. Ann. Int. Med. 90:53-54, 1979.

3. Corash, L., Spielberg, S., Bartsocas, C., Boxer, L., Sheetz, M., Steinherz, R., Schulman, J.D.: Reduced Chronic Hemolysis in Mediterranean Glucose-6-Phosphate Dehydrogenase Deficiency After Vitamin E Therapy. Clin. Res. 27:291A, 1979.

4. Schulman, J.D., Corash, L., Bartsocas, C., Spielberg, S., Boxer, L., Sheetz, M., Steinherz, R. and Papadatos, C.: Reduced Chronic Hemolysis in Mediterranean Glucose-6-Phosphate Dehydrogenase Deficiency After Vitamin E Therapy. Proc. of the Second International Clinical Genetics Seminar: Management of Genetic Disorders (Athens, Greece), A.R. Liss, Inc., New York, June 4-7, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF **INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10030-02 |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Terminal Deoxynucleotidyl Transferase Assays and Disease Correlations

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Fred Bollum | Chairman, Biochemistry Dept., | USUHS |
| | Dr. David Poplack | Staff, Pediatric Oncology, | NCI |
| | Dr. Greg Reaman | Clinical Associate, Pediatric Onc. | NCI |

COOPERATING UNITS (if any)

Pediatric Oncology Branch, NCI
Department of Biochemistry, USUHS

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 0.6 | PROFESSIONAL: 0.4 | OTHER: 0.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Terminal deoxynucleotidyl transferase (TdT) has been shown to be an effective biochemical marker for lymphoblastic cells in normal thymus acute lymphoblastic leukemia (ALL) and lymphoblastic leukemias. The enzyme TdT can be assayed for as an enzyme activity or by an indirect fluorescent antibody procedure. This current project attempted to compare the sensitivity of the two methods of determining the TdT enzyme. In addition, peripheral blood smears, bone marrow aspirate smears and cytocentrifuge slide preparations from a wide variety of diseases as well as normal donors were surveyed for TdT to determine its level in various diseases. Attempts at developing a PAP immunohistochemical assay for localizing TdT in tissue sections was unsuccessful.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL-10030-02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial Number: Z01 CL-10030-01 CP
Project Title: Terminal Deoxynucleotidyl Transferase Assays and Disease Correlations

Principal Investigator: Dr. Jerome A. Donlon

Other Investigators: Dr. Fred Bollum
Dr. David Poplack
Dr. Greg Reaman

Man Years:

| | |
|---|---|
| Total: | 0.6 |
| Professional: | 0.4 |
| Other: | 0.2 |

## Project Description

### Objectives:

1. To establish the validity and usefulness of an indirect fluorescent antibody assay for TdT as compared to the enzyme activity assay.

2. To obtain a broad experience with TdT assays to assess its clinical relevance in diagnosis and prognosis of various diseases.

### Methods Employed:

1. Indirect fluorescent antibody procedure for peripheral blood, bone marrow aspirate and cytocentrifuge smears.

2. Enzyme activity assay for TdT by radioisotope tracer incorporation.

### Findings:

1. Indirect fluorescent antibody assays and enzyme activity assays show comparable sensitivities for TdT.

2. The TdT activity is decreased and often undetectable in T cell ALL as compared to the high TdT activity found in common (null cell) ALL.

3. Occasional slight elevations of TdT activity have been noted in bone marrow aspirations from patients with rhabdomyosarcoma.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10031-02 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

A Clinico-Pathologic Study of the Hypereosinophilic Syndrome

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Morris Flaum | Clinical Associate, Hematology Service | CP CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, | CP CC |
| | Dr. Anthony Fauci | Staff, Lab. Clinical Investigation | |
| | Dr. Robert Schooley | Chief Clinical Associate | NIAID |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3 | 3 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The bone marrows of patients seen at the Clinical Center with Hypereosinophilic Syndrome were reveiwed. This was done in an attempt to correlate the bone marrows and other hematologic parameters with the patient's clinical course and response to therapy.

PHS-6040
(Rev. 10-76)

NUCLEAR MED.
MED. REC.
FABRIC CARE
ESCD
DIAG. RADIOL.
PHARMACY

Project No. Z01 CL-10031-02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979
Previous Serial Number: Z01 CL-10031-01 CP
Project Title: A Clinico-Pathologic Study of the Hypereosinophilic Syndrome

Principal Investigator: Dr. Morris A. Flaum

Man Years:

| | |
|---|---|
| Total: | 3 |
| Professional: | 3 |
| Other: | |

## Project Description

### Objectives:

To determine whether hematologic manifestations of the hypereosinophilic syndrome can be used to correlate with 1) the clinical course of the patient and, 2) response to therapy.

### Methods Employed:

The bone marrows of 32 patients were reviewed microscopically. All other hematologic data were also systematically reviewed.

### Major Findings:

Patient subgroups, defined by response to therapeutic intervention, can be predicted by initial hematologic evaluation.

### Significance:

Since a patient's response to therapy, and thus prognosis, can be defined at initial evaluation, more rational therapeutic intervention can be planned. Alternatives to present management can also be considered.

### Proposed Course:

Clinical correlates with response to therapy are being determined and will be correlated with the hematologic classification.

### Honors and Awards:

None

Publications: None

Significance:

1. The indirect fluoresecent antibody assay is sensitive and easily applied to routinely obtained slide specimens.

2. The T cell ALL has a poorer clinical prognosis, therefore in addition to the surface marker, a low or absent TdT activity would confirm this poor prognosis. Possibly chemotherapy protocols can be adjusted if an ALL is found to be a T cell or low TdT type.

3. High TdT activity is possibly associated with more primitive lymphoblasts, whereas the low TdT activity may occur as the cell becomes more differentiated, expressing the T surface marker.

Honors and Awards:

None

Publications:

None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-10032-02 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)
NEW TITLE:
The Localization and Functional Significance of Platelet Membrane-Bound Factor VIII

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Morris A. Flaum | Clinical Associate, Hematology Ser., CP | CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CP | CC |
| | Dr. Margaret E. Rick | STaff, Hematology Service, CP | CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 2.0 | |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The role of platelet membrane-bound factor VIII is being pursued by using a factor VIII antibody as a probe. Antibodies to the low molecular weight and high molecular weight fragments of factor VIII localized by immunofluorescence. The functional significance of these fragments is then determined by platelet aggregometry with ristocetin.

PHS-6040
(Rev. 10-76)

Project No. Z01-CL-10032-02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial Number: Z01-CL-10032-01 CP

Project Title: The Localization and Functional Significance of Platelet Membrane-Bound Factor VIII

Principal Investigator: Dr. Morris A. Flaum

Other Investigators: Dr. Harvey R. Gralnick
Dr. Margaret E. Rick

Man Years:

| | |
|---|---|
| Total | 2.0 |
| Professional: | 2.0 |
| Other: | |

## Project Description

Objectives:

To determine the role of platelet membrane-bound factor VIII.

Methods Employed:

The localization and determination of the functional significance of factor VIII is being pursued by using factor VIII antibodies as probes. The antibodies, produced in humans, goats, and rabbits, are incubated with fresh or formalinized platelets and immunofluorescence performed. The antibodies have been demonstrated to react with either the low or high molecular weight fragments in other systems. Ristocetin cofactor activity is determined by tilt-tube and aggregometry with platelets pre-incubated with these antibodies.

Major Findings:

Preliminary studies suggest that the antibodies react with platelet membrane-bound factor VIII, but that there is no inhibition of von Willebrand factor activity after pre-incubation with platelets.

Significance:

The role of platelet membrane-bound factor VIII is unknown. Clarification of its role will increase understanding of platelet function in hemostasis. This may lead to new insights of the interaction of platelets with the coagulation sequence and platelet dysfunction in von Willebrand's disease.

Proposed Course:

Further studies to clarify the functional significance of platelet membrane bound factor VIII are now actively being pursued.

Honors and Awards:

None

Publications:

None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10033-02 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

The Effect of Plasmapheresis on Coagulation

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Morris A. Flaum | Clinical Associate, Hematology Service | |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CP CC | |
| | Dr. Richard Cuneo | Clinical Associate, Neurology | NINCDS |
| | Dr. W. King Engel | Staff, Neurology Brance | NINCDS |
| | Dr. Frederick Applebaum | Staff, Pediatric Oncology | NCI |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Dept., Clinical Center

SECTION
Hematology Service

INSTITUTE AND LOCATION
CP, CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | .75 | .75 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The effect of plasmapheresis on coagulation was determined by sampling patients prior to, immediately after, and 24 hours after, plasmapheresis. Coagulation studies were then performed on these specimens as well as the plasma removed.

Project No. Z01 CL 10033-02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: The Effect of Plasmapheresis on Coagulation

Principal Investigator: Dr. Morris A. Flaum

Man Years:

| | |
|---|---|
| Total: | 1.5 |
| Professional: | .75 |
| Other: | .75 |

## Project Description

### Objectives:

To determine the effect of plasmapheresis on coagulation factors.

### Methods Employed:

Patients were sampled prior to, immediately, 4 hours after, and 24 hours after plasmapheresis. Routine coagulation studies were then performed on these specimens as well as on the plasma removed. Special studies included anti-thrombin III levels and fibrinogen levels by Clauss, Ratnoff-Menzie and immunologic methods, clotting factor assays, factor VIII antigen levels, and von Willebrand factor activity.

### Major Findings:

Serial studies revealed that immediately after the exchange transfusion, there was significant prolongation of the prothrombin, partial thromboplastin and thrombin times with reduction of the fibrinogen and antithrombin III levels. Factors V, VII-X, IX and X were all significantly decreased, as were the factor VIII antigen, procoagulant and the ristocetin cofactor. Platelet counts were obtained before and after 34 exchanges and revealed significant decreases. Four hours after exchange, all parameters remained abnormal except the factor IX, ristocetin factor and factor VIII procoagulant activity. By 24 hours, all hemostatic parameters had returned to normal.

Significance:

Plasma exchange is a new modality of therapy with possible application to multiple disorders. Its effects on man's homeostasis is unknown. This study will allow us to gain insight into the effect of plasma exchange on coagulation.

Proposed Course:

The study had been completed save for further evaluation and laboratory analysis of changes in factor VIII.

Honors and Awards:

None

Publications:

Flaum, M.A., R.A. Cuneo, F. R. Appelbaum, A.B Deissrath, W.H. Eyel, H.R. Gralnick. The Hemostatic Imbalance of Plasma Exchange Transfusion. Blood 52 (Suppl. 1): 298, 1978 (Abstract)

SMITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CL 10034-02 CP

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Thrombin Activation of Factor VIII

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Margaret E. Rick | Staff Physician | CP CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department, Clinical Center

SECTION
Hematology Service

INSTITUTE AND LOCATION
CP, CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 0.50 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This investigation seeks to characterize the interaction of the factor VIII complex with thrombin, in particular the biochemical mechanism by which thrombin activates factor VIII procoagulant activity and subsequently inactivates the activity. An understanding of the regulatory role of this interaction in normal hemostasis will lead to a better understanding of the basic hemostatic process and of the functional defects in the factor VIII deficiency diseases (Hemophilia A and von Willebrand's disease) as well as in pathologic thrombotic states.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10034-02 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979
Previous Serial Number: Z01 CL 10034-01 CP
Project Title: Thrombin Activation of Factor VIII

Principal Investigator: Dr. Margaret E. Rick

Man Years:

| | |
|---|---|
| Total: | 1.5 |
| Professional: | 0.50 |
| Other: | 0.75 |

## Project Description

### Objectives:

To characterize the biochemical interaction of thrombin and factor VIII and relate this to the functional change in factor VIII procoagulant activity.

### Methods Employed:

Purified human factor VIII is obtained by differential PEG precipitation of factor VIII concentrates followed by agarose gel filtration. A low molecular weight factor VIII procoagulant is obtained by gel filtration of purified factor VIII buffers containing 0.24 M $CaCl_2$. Thrombin interaction with the factor VIII preparations is assessed with factor VIII procoagulant assays. Inhibitors of thrombin (hirudin, DFP, heparin) are employed in studying various aspects of the interaction.

### Major Findings:

The reaction patterns of thrombin with purified factor VIII and the calcium dissociated low molecular weight factor VIII are similar, demonstrating an initial increase in factor VIII activity followed by a decay of procoagulant activity. The extent of activation which is observed in the initial phase decreases with lower temperatures and with lower thrombin concentrations. A pseudo-first order relationship is demonstrated for the activation phase. The labile factor VIII procoagulant activity produced by thrombin action cannot be stabilized by the addition of inhibitors of thrombin and thus appears to be intrinsically labile. Further studies have indicated that there is product inhibition of the reaction of thrombin with factor VIII.

Significance to Biomedical Research and the Program of the Department:

The goal of this research is to gain a better understanding of the function of factor VIII in normal hemostasis, in factor VIII deficiency diseases, and in pathologic thrombotic states. The important regulatory role of thrombin in factor VIII function will lead to a better understanding of regulation in normal hemostasis and may allow therapeutic manipulation by pharmacologic agents in thrombotic diseases.

Honors and Awards:

None

Publications:

1. Rick, M.E., and Hoyer, L.W.: Immunologic Studies of Antihemophilic Factor (AHF, Factor VIII). V. Immunologic Properties of AHF Subunits Produced by Salt Dissociation. Blood 42:737-747, 1973.

2. Rick, M.E., and Hoyer, L.W.: Thrombin Activation of Low Molecular Weight Antihemophilic Factor (Factor VIII). Nature 252:404, 1974.

3. Rick, M.E., and Hoyer, L.W.: Interaction of thrombin and factor VIII; I. The Role of Protease Inhibitors. Br. J. Haematol. 36:585-597, 1977.

4. Mundy, G.R., Rick, M.E., Turcotte, B.A., Kowalski, M.A.: Hypercalcemia in Lymphosarcoma Cell Leukemia. Am. J. Med. 65:600-605, 1978.

5. Rick, M.E., and Hoyer, L.W.: Thrombin Activation of Factor VIII; II. A comparison of purified factor VIII and the low molecular weight factor VIII procoagulant. Br. J. Haematol. 38:107-119, 1978.

6. Rick, M.E.: Biochemistry of Blood Coagulation, in The Science and Practice of Clinical Medicine, Chapt. 75, V.J. Marder (ed.), Grune and Stratton, Inc., New York, 1979.

7. Rick, M.E.: Hemophilia and von Willebrand's Disease, in The Science and Practice of Clinical Medicine, Chapt. 80, V.J. Marder (ed.), Grune and Stratton, Inc., New York, 1978.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10035-02 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Factor VIII Interaction with other Coagulation Factors

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Margaret E. Rick | Staff Physician | CP CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Dept., Clinical Center

SECTION
Hematology Service

INSTITUTE AND LOCATION
CP, CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.25 | 0.25 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This project seeks to investigate the interaction of factor VIII with other coagulation factors, particularly with factor IX$_a$, calcium, and phospholipid in the quaternary complex formed by these factors. The importance of protolytic activation of factor VIII prior to its participation in the complex will be assessed, and the nonfunctional factor VIII molecule present in patients with Hemophilia A will be studied to determine whether it can participate in the quaternary complex.

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Project Number: Z01 CL 10035-01 CP
Project Title: Factor VIII Interaction with other Coagulation Factors.

Principal Investigator: Dr. Margaret E. Rick

Man Years:

| | |
|---|---|
| Total: | 0.5 |
| Professional: | 0.25 |
| Other: | 0.25 |

## Project Description

### Objectives:

To characterize the interaction of factor $IX_a$ with factor VIII and the low molecular weight factor VIII procoagulant, assessing any "activation" of factor procoagulant activity by factor $IX_a$ and developing an affinity reagent to study components of the quaternary complex (factor VIII, factor $IX_a$, calcium, phospholipid).

### Methods Employed:

Purified human factor VIII is obtained by differential PEG precipitation of factor VIII concentrates followed by agarose gel filtration. A low molecular weight factor VIII procoagulant is obtained by gel filtration of purified factor VIII with buffers containing 0.24 M $CaCl_2$. Factor IX is purified by barium citrate adsorption and elution, ion exchange chromatography, and affinity chromatography. Activation of factor VIII is assessed by procoagulant assay and the quaternary complex will be assessed using solid phase factor IX as an affinity reagent.

### Major Findings:

Preliminary studies indicate that factor $IX_a$ does not activate factor VIII in a purified system.

Significance to Biomedical Research and the Program of the Department:

The goal of this research is to gain a better understanding of the function of factor VIII in normal hemostasis and in the factor VIII deficiency diseases (Hemophilia A and von Willebrand's Disease). The role of the respective components within the quaternary complex will provide insights into the normal function of factor VIII and the possible mechanism of dysfunction in the factor VIII deficiency diseases.

Honors and Awards:

None

Publications:

None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10036-02 |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)
Evaluation of the Limulus Lysate Test

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Ronald J. Elin, Chief, Clinical Pathol. Dept., CC

Others: Harold Nishi, Senior Staff, Chemistry Service, CPD,CC

COOPERATING UNITS (if any)
None

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, Maryland 20014

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The limulus lysate test is currently the most sensitive assay for the detection of bacterial endotoxin. The sensitivity and specificity of the limulus test for the detection of bacterial endotoxin in blood, cerebral spinal fluid, joint fluid and urine in man have been and are being evaluated to determine the clinical utility of this assay. Compounds other than bacterial endotoxin that can cause a positive limulus reaction are being characterized. A nephelometric method for performing the limulus assay to enhance sensitivity and specificity is being developed.

[illegible]-6040
(Rev. 10-76)

Project No. Z01 CL 10036-02
1. Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 to September 30, 1979

Project Title: Evaluation of the Limulus Lysate Test

Previous Serial No.: Z01 CL 10036-01

Principal Investigator: Dr. Ronald J. Elin

Other Investigator: Mr. Harold Nishi

Cooperating Units: None

Man Years: Total 1.0
Professional 0.25
Other 0.75

## Project Description

Objectives:

To determine the specificity, clinical utility and optimum method for performance of the limulus assay.

Methods Employed:

The limulus assay was performed by mixing lysate with the test material and determining if gelation occurred. The assay was also performed using a nephelometer.

Major Findings:

The limulus assay is not specific for the detection of bacterial endotoxin in joint fluid or plasma from humans. The test does have clinical utility for the detection of bacterial endotoxin in cerebral spinal fluid. It appears that an elevated neutrophil count may affect a positive limulus test.

Significance:

The use of the limulus test for the detection of bacterial endotoxin in plasma in joint fluid is not recommended. The test does have clinical utility for the detection of bacterial endotoxin in cerebral spinal fluid.

Honors and Awards: None

Publications:

Hochstein, H. D., Elin, R. J., Cooper, J. F., Seligman, E. B., Jr., and Wolff, S. M.: Further developments of limulus anebocyte lysate test. Bull. Parenteral Drug Assoc: 27: 139-148, May-June 1973.

Elin, R. J., Robinson, R. A., Levine, A. S., and Wolff, S. M.: Lack of clinical usefulness of the limulus test for the diagnosis of endotoxemia. N. Engl. J. Med. 293: 521-524, September 1975.

Elin, R. J., Sandberg, A. L., and Rosenstreich, D. L.: Comparison of the pyrogenicity, limulus activity, mitogenicity and complement reactivity of several bacterial endotoxins and related compounds. J. Immunology. 117: 1238-1242, October 1976.

Elin, R. J., Knowles, R., Barth, W. F., and Wolff, S. M.: Lack of specificity of the limulus lysate test in the diagnosis of pyrogenic arthritis. J. Infect. Dis. 137: 507-513, 1978.

Elin, R. J.: Clinical utility of the limulus test with blood, CSF and synovial fluid. In Cohen, E. (ed.): Biomedical Applications of Limulus Polyphemus. Alan R. Liss, Inc., New York. 1979.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10037-02 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Adherence of Bacteria, Blood Cells and Other Particles to Large Porosity Membrane Filters. (continuing study)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Charles H. Zierdt, Microbiologist, Microbiology Service, CPD, CC

OTHERS: Students taking University of Maryland course 388 (Special Topics, or "internship")

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.25 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Membrane filters with pore sizes much larger than bacteria, 1,2,3,5,8,10, and 14 micra diameter, will effectively remove those bacteria from filtered suspensions. The phenomenon depends on surface charge, intrinsic to membrane filters and probably a by-product of the manufacturing process. Membrane filters of any material possess the charged surfaces, but cellulose and cellulose acetate polymers have more than polycarbonate filters, and thereby are more attractive to bacteria. Gram-positive organisms are attracted more than Gram-negative. Nylon, Teflon, and vinal membrane filters are far less "magnetic." Bacteria continue to attach to a membrane until a dense monolayer of particles is formed. For a 47 mm diameter cellulosic filter, roughly 1 x 10 bacterial cells are required to "saturate" the filter on continued filtration. Then a much larger percent of the bacteria pass through the filtrate, but never 100% and eventually they pile up on the filter sufficiently to slow filtration by blocking the pores. Tween 20 (0.05%), a nonionic detergent, elutes at least half of the particles with one 50 ml volume, and all particles upon repeated elution.

PHS-6040
(Rev. 10-76)

NUCLEAR MED.
MED. REC.
FABRIC CARE
ESCD
DIAG. RADIOL.
PHARMACY

Project No. Z01 CL-10037-02 CP
1. Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Adherence of Bacteria, Blood Cells and Other Particles to Large Porosity Membrane Filters

Previous Serial No.: Z01 CL-10037-01 CP

Principal Investigator: Dr. Charles H. Zierdt
Other Investigators: Students, taking University of Maryland course 388 (Special Topics, or "internship").

Man Years:
Total: 1.0
Professional: 0.25
Other: 0.75

## Project Description

### Objectives:

To work out the basics of the phenomenon described, to attempt to develop ways of reversing the phenomemon (getting particles back off the filters), and to report this in an appropriate journal (Science).

### Methods Employed

The usual filtration techniques, with appropriate commercial filters apparatus and membranes. The use of various tween compounds (nonionic) to effect detachment of adherent particles.

### Honors and Awards:

None

### Publications:

Presentation: Zierdt, C.H. 1978. Unexpected adherence of bacteria, blood cells, and other particles to large porosity membrane filters. Annual meeting of the American Society for Microbiology, Microbiologica Abstracts, p. 210.

In Press: Adherence of bacteria, yeast, blood cells and latex spheres to large porosity membrane filters.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10038-02 CP |

PERIOD COVERED
October 1, 1978 through September 30 1979

**TITLE OF PROJECT (80 characters or less)**

Identification of Alpha Hemolytic and Non-Hemolytic Streptococci

**NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT**

PI: Dr. Vee J. Gill, Supervisory Microbiologist, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.75 | 0.25 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

**SUMMARY OF WORK (200 words or less - underline keywords)**

Group D streptococci and alpha hemolytic and non-hemolytic streptococci isolated from blood and other sterile fluid sites from Clinical Center patients were collected and speciated. Speciation of these streptococci has defined which species are of greater significance in infection of compromised hosts.

Project No. Z01 CL-10038-02 CP
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Identification of Alpha Hemolytic and Non-hemolytic Streptococci

Previous Serial No.: Z01 CL-10038-01 CP

Principal Investigator: Dr. Vee J. Gill
Other Investigator: None

Man Years:
Total: 1.0
Professional: 0.75
Other: 0.25

## Project Description

### Objectives:

To define the role of different species of Group D, alpha, and non-hemolytic streptococci as infecting agents of compromised hosts.

### Methods:

Alpha and non-hemolytic streptococci isolated from blood or other sterile fluids are evaluated for their biochemical and antibiotic sensitivity characteristics. Identification has been facilitated by adapting a miniaturized biochemical evaluation strip (ana - API) for more rapid results.

### Major Findings:

Most isolates can be identified as one of the 15 recognized species of Group D, alpha or non-hemolytic streptococci. Amongst Group D streptococci, the fact that S. faecium represents 30% of presumptive Group D isolates is unexpected. The species seen most frequently amongst alpha and non-hemolytic are S. mitis (27), S. intermedium (20), and S. sanguis II (21). This distribution differs from that seen in studies of the various species in cases of endocarditis, and also organisms referred to CDC.

Significance:

Sepsis and other serious infection with gram positive organisms seen to be increasing in importance in patients at the Clinical Center. Knowledge of the specific species involved is necessary in order to understand the pathogenesis of these infections.

Proposed Course:

The project has been completed and information is now being compiled for publication.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10043-01 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Hydroperoxidase Stain for Phi Bodies

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CP | CC |
| | Dr. Jacob S. Hanker | Dental Research Center, Un. of NC<br>Chapel Hill, NC | |

COOPERATING UNITS (if any)

Dental Research Center, University of North Carolina, Chapel Hill, NC

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 0.1 | PROFESSIONAL: 0.1 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A recently published hydroperoxidase special stain procedure allegedly demonstrated small "phi-body" like cytoplasmic inclusions which were seen almost exclusively in leukocytes from acute myelogenous leukemia (AMML). These inclusions appeared in increased numbers and in more cells than the previously well known marker Auer rod. The phi bodies are much smaller than Auer rods. Their increased frequency may be a histochemical marker for disease or early relapse in AML or AMML. The purpose of our current study was to evaluate the usefulness of the hydroperoxidase stain and the relatedness of phi bodies in disease detection.

PHS-6040
(Rev. 10-76)

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10043 01 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Hydroperoxidase Stain for Phi Bodies

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CP | CC |
| | Dr. Jacob S. Hanker | Dental Research Center, Un. of NC<br>Chapel Hill, NC | |

COOPERATING UNITS (if any)
Dental Research Center, University of North Carolina, Chapel Hill, NC

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>0.1 | PROFESSIONAL:<br>0.1 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A recently published hydroperoxidase special stain procedure allegedly demonstrated small "phi-body" like cytoplasmic inclusions which were seen almost exclusively in leukocytes from acute myelogenous (AMML). These inclusions appeared in increased numbers and in more cells than the previously well known marker Auer rod. The phi bodies are much smaller than Auer rods. Their increased frequency may be a histochemical marker for disease or early relapse in AML or AMML. The purpose of our current study was to evaluate the usefulness of the hydroperoxidase stain and the relatedness of phi bodies in disease detection.

Project No. Z01 CL 10043 01 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Hydroperoxidase Stain for Phi Bodies
Previous Serial No.: None
Principal Investigator: Dr. Jerome A. Donlon

Other Investigators: Dr. Harvey R. Gralnick
Dr. Jacob S. Hanker

Man Years:

| | |
|---|---|
| Total: | 0.1 |
| Professional: | 0.1 |
| Other: | |

## Project Description

### Objectives:

To verify a special histochemical stain for phi bodies which may allow a more sensitive detection of disease.

### Methods Employed:

Hydroperoxidase stain procedure of Jacob Hanker; a 15-minute procedure utilizing air-dried peripheral blood or bone marrow smears.

### Major Findings:

Bone marrow aspirate smears and peripheral blood smears from normal donors and several patients each with AML with Auer rods; AML without Auer rods; APL with Auer rods, CGL in myeloblast crisis without Auer rods and AMML without Auer rods were processed in duplicate by the hydroperoxidase stain procedure. In no case did the phi body stain detect phi bodies where no Auer rods were seen. In those cases where Auer rods were seen on the Wrights stain, the phi bodies were also demonstrated by the special stain.

### Significance:

The significance of phi bodies as demonstrated by the hydroperoxidase stain is not clear. They may represent pre-Auer rods. Although the demonstration of phi bodies is of interest, it adds no additional diagnostic information. It does not warrant technologist time for preparation or evaluation. A careful search of the Wright stain smears should yield adequate Auer rods if present ot confirm a diagnosis.

Honors and Awards:

None

Publications:

None

|  |  |  |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10044 01 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Lysis-filtration Blood Culture Technique

**NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT**

PI: Dr. Charles H. Zierdt, Microbiologist, Microbiology Service CPD, CC

OTHER: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.25 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This new technique and the conventional blood culture technique are currently being compared, specimen for specimen, although not all samples are lysed for culture. The present benign lysing solution is non-injurious to most pathogens, and indeed forms a superior growth medium for many. But it contains 0.04% Triton x-100, which adversely affects some pathogens. Tween 20 (polyoxyethylene sorbitan monolaurate) was tested to replace Triton x-100, and was discovered to be non-toxic, even to Neisseria meningitidis, while lysing blood cells adequately, in 2% concentration. Testing should be complete in the next few months.

PHS-6040
(Rev. 10-76)

Project No. ZO CL 10044 01
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial No.: None

Project Title: Lysis-Filtration Blood Culture Technique (con't study.)

Principal Investigator: Dr. Charles H. Zierdt
Other Investigator: Dr. James D. MacLowry
Cooperating Units: None

Man Years:
Total: 1.0
Professional: 0.25
Other: 0.75

## Project Description

### Objectives:

Continue to develop and improve the existing successful technique for this radically different blood culturing technique. In addition to collecting data from clinical studies, animal studies are in progress to provide controlled experiments comparing the relative abilities of the conventional and the lysis filtration blood culture techniques to recover pathogenic microorganisms from blood.

### Methods Employed:

Lysis of blood with a solution containing either Triton X-100 or Tween 20 and subsequent filtration of blood and incubation of filter pad.

### Honors and Awards:

None

### Publications:

Zierdt, C. H., Kagan, R. L. and MacLowry, J. D.: Development of a Lysis-Filtration Blood Culture Technique. J. Clin. Microbiol. 5: 46-50, 1977.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10045 01 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Evaluation of Throat Gram Smears

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Vee L. Gill, Supervisory Microbiologist, Microbiology Service, CPD, CC

OTHER: Dr. Frank G. Witebsky, Asst. Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.75 | 0.25 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Throat swabs submitted for routine culture had Gram stains performed on them also. These were read without prior knowledge of cultural results and scored for the presence or absence of group A-beta hemolytic streptococcal infection, using the criteria of Crawford, et.al. (Ann. Int. Med., 90: 293-297, 1979.)

PHS-6
(Rev.

Project No. Z01 CL 10045 01 CP
1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Evaluation of Throat Gram Smears

Previous Serial No.: None

Principal Investigator: Dr. Vee L. Gill
Other Investigators: Dr. Frank H. Witebsky

Man Years:
Total: 0.5
Professional: 0.75
Other: 0.25

## Project Description

Objectives:

To determine the usefulness of the throat gram stain as a predictor of streptococcal sore throat.

Methods Employed:

Criteria of Crawford et.al. were used. All throat swabs submitted for routine culture also had smears done. These smears were collected and read independently by one microbiologist and one clinical pathologist.

Significance to Biomedical Research and the Program of the Institute:

Since the publication of Crawford et. al., the laboratory has had questions regarding the potential use of this rapid technique for predicting streptococcal pharyngitis. Such a technique needs verification by other independent investigators to corroborate or oppose their recommendations. Use of this technique has large potential financial, as well as medical considerations of significance to the community.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10046 01 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Significance of Anaerobic Bacteria from Patient Specimens

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Vee L. Gill, Supervisory Microbiologist, Microbiology Service, CPD, CC

OTHER: Dr. Kathleen Sazama, M.D., Clinical Pathology Resident, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1 | 0.75 | 0.25 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients from whom anaerobic bacteria are isolated will have their charts reviewed and physicians consulted to determine the clinical significance of the isolates. Follow-up will include the nature of the treatment, if any, and clinical response. These results should guide our laboratory as well as others to determine how much anaerobic work is necessary for optimum patient care.

PHS-6
(Rev.

Project No. Z01 CL 10046 01 CP

1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Significance of Anaerobic Bacteria from Patient Specimens

Previous Serial No.: None

Principal Investigator: Dr. Vee L. Gill
Other Investigator: Dr. Kathleen Sazama

Man Years:
  Total: 1
  Professional: 0.75
  Other: 0.25

## Project Description

### Objectives:

To assess the significance of anaerobes isolated from patient specimens. Information is needed regarding the specific organisms and their role in infection, as well as the clinical usefulness of providing anaerobic culturing.

### Methods Employed:

All wounds, abscesses, lesions and drainage materials are cultured for anaerobes. Full anaerobic work-up is done on most anaerobes isolated. Patients' charts will be reviewed and their physician spoken with, when relevant, to determine the role of these anaerobes.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10047 01 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Correlations of Methods for Determining Penicillin Resistance

**NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT**

PI: Dr. Vee L. Gill, Supervisory Microbiologist, Microbiology Service, CPD, CC

OTHER: Ms. Carol Manning, M.T. (ASCP)
Ms. Colleen Ingalls, M.T. (ASCP)

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.75 | 0.25 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Isolates of staphylococcus aureus and S. epidermidis were examined for penicillin sensitivity or resistance using the following criteria: 1) MIC, 2) inhibition zone size, 3) nature of the zone edge, and, 4) penicillinase assay. Results indicate that the MIC's and nature of the zone edge are good predictors of resistance although a small per cent of isolates with "sensitive" MIC's were found to be penicillinase producers. Absolute zone size criteria showed most "Intermediate" zones to be penicillinase producers.

Project No. Z01 CL 10047 01 CP

1. Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Correlations of Methods for Determining Penicillin Resistance

Previous Serial No.: None

Principal Investigator: Dr. Vee L. Gill
Other Investigators: Ms. Carol Manning, M.T. (ASCP)
Ms. Colleen Ingalls, M.T. (ASCP)

Man Years:
Total: 1.0
Professional: 0.75
Other 0.25

## Project Description

### Objectives:

1) To determine the extent of false "sensitive" MIC's by the microtiter dilution technique. 2) To determine if either interpretation of zone size or zone edge would be useful adjunctive predictors of penicillinase production.

### Methods Employed:

All staphylococci submitted for sensitivity testing were simultaneously set-up to check plate with penicillin and oxacillin discs. Zone sizes and nature of zone edge were recorded. Penicillinase testing using a phenol red-penicillin assay method was done from the same check plate.

### Major Findings:

These are currently being summarized (see preceeding page) and will be prepared for publication.

### Proposed Course:

See above

### Publications:

None

NUCLEAR MED.
MED. REC.
OCC. MED.
FABRIC CARE
OPD
ESCD
DIAG. RADIOL.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10048 01 CP |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Evaluation of a Simplified Disc Antibiotic Susceptibility Test

**NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT**

PI: Dr. Frank G. Witebsky, Asst. Chief, Microbiology Service, CPD, CC

OTHER: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)
None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.2 | 0.1 | 0.1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Antibiotic susceptibility testing is most commonly performed using a disc diffusion method. The procedure requires extremely careful standardization and quality control, and diameters of zones of inhibition around the discs are often difficult to read because of the manner of plate inoculation. A simplified procedure of inoculum preparation, which also provides zone edges which are much easier to read, is under investigation and is being compared with the standard procedure.

Project No. Z01 CL 10048 01 CP

1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Evaluation of a Simplified Disc Antibiotic Susceptibility Test

Previous Serial No.: None

Principal Investigator: Dr. Frank G. Witebsky
Other Investigator: Dr. James D. MacLowry

Man Years:
Total: 0.2
Professional: 0.1
Other: 0.1

## Project Description

### Objectives:

The objective of this study is the development and evaluation of a simplified disc diffusion antibiotic susceptibility testing procedure, in which the inoculum will be easier to prepare and the edges of the zones of inhibition will be easier to read.

### Methods Employed:

Antibiotic susceptibility testing plates are flooded with a 1:1000 dilution of a turbid broth suspension of the organisms to be tested; residual broth is aspirated from the plates and the usual susceptibility testing discs are applied. Zones of growth inhibition are read after 18-24 hours of incubation at 37°C. Parallel testing using the same organisms is performed using the standard Bauer-Kirby procedure. When sufficient data has been accumulated, the correlation of the two procedures will be assessed.

### Major Findings:

Insufficient data has been accumulated thus far for analysis. This procedure has already been found useful as a part of our susceptibility testing procedures (1), but the disc testing aspect was not directly correlated with the standard procedure, and the interpretive criteria presently used are too complex for general use.

Significance to Biomedical Research and the Program of the Institute:

Should this procedure prove widely usable, it will simplify the most commonly employed antibiotic susceptibility testing procedure used in this country. A considerable saving in technologist time may accrue, as well as increased reliability of test results.

Proposed Course:

See above

Publications:

MacLowry, J. D., M. J. Jaqua, and S. T. Selepak. Detailed methodology and implementation of a semiautomated serial dilution microtechnique for antimicrobial susceptibility testing. Appl. Microbiol. 20: 46-53, 1970.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10049 01 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Evaluation of a New Procedure for Identification of Enterobacteriaceae

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Frank G. Witebsky, Asst. Chief, Microbiology Service, CPD, CC

OTHER: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.3 | 0.1 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Gram negative rods belonging to the genus Enterobacteriaceae are among the most common human pathogens. Even with the use of new miniaturized systems, their identification continues to take up a considerable amount of laboratory time and resources. Using microtitration plates prepared in-house with commercially available media, we will explore the feasibility of such plates for organism identification, with the goal of determining whether such a procedure can be made adequately accurate, yet less costly than other currently available procedures.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10049 01 CP

1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Project No.: None

Project Title: Evaluation of a New Procedure for Identification of Enterobacteriaceae

Previous Serial No: None

Principal Investigator: Dr. Frank G. Witebsky
Other Investigator: Dr. James D. MacLowry

Man Years:
Total: 0.3
Professional: 0.1
Other: 0.2

## Project Description

### Objectives:

The objective of this study is the evaluation of media commercially prepared by the Dynatech Corporation for identification of organisms belonging to the genus Enterobacteriaceae, which includes many common human pathogens. We will investigate whether a procedure can be devised, and a set of biochemicals selected, so that adequate accuracy of species identification can be attained at a cost less than that of currently available miniaturized systems.

### Methods Employed:

Using the Dynatech MIC-2000 96 channel dispenser and media prepared by Dynatech, plates containing selected biochemicals will be prepared in-house. The cost and accuracy of this system will be compared with that of the API-20E system currently used in our laboratory.

### Major Findings:

The project has just begun.

### Significance to Biomedical Research and the Program of the Institute:

All currently available methods for accurate identification of members of the genus Enterobacteriaceae are relatively costly. Any procedure which might decrease this cost would be useful to our institution and potentially useful to others as well.

## Proposed Course:

See above

## Publications:

None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10050 01 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Interactions of Cold Insoluble Globulin with Coagulation Proteins

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Craig M. Kessler | Staff, Hematology Service, CP | CC |

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department

SECTION

Hematology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.9 | 0.5 | 0.4 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Cold insoluble globulin (CIg), also known as fibronectin, is a major glycoprotein of vertebrate blood and organ stroma. Fibroblasts and endothelial cells in cell culture synthesize CIg and may act as the sources of circulating CIg in vivo. CIg apparently interacts with platelets, fibrinogen and coagulation factor XIII in vitro; however, its physiologic significance and function have not been established. Many of the existing methods to isolate CIg for study were inadequate. An efficient technique has been examined to purify CIg in large quantities and to render it free of contaminating coagulation proteins and inhibitors. This technique will also provide a means to analyze the interactions between purified coagulation proteins and CIg.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10050 01

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Interactions of Cold Insoluble Globulin with Coagulation Proteins
Previous Serial No.: None
Principal Investigator: Craig M. Kessler, M.D.

Man Years:

| | |
|---|---|
| Total | 0.9 |
| Professional: | 0.5 |
| Other: | 0.4 |

## Project Description

### Objectives:

1. Purification of CIg which is structurally and functionally intact and free of contaminating proteins, which participate in coagulation.

2. Development of an in vitro assay of CIg function based on its interaction with coagulation proteins.

3. Examination of CIg as a mediator of platelet aggregation, coagulation protein activation and post-ribosome coagulation protein assembly.

4. Examine the proteolytic fragmentation of CIg by trypsin, plasmin and thrombin. This will provide information regarding molecular structure and may provide a kinetic toll for comparing structures of cell surface bound CIg with circulating CIg.

### Methods Employed:

CIg is purified by passing fresh human plasma over a gelatin affinity column. Proteolytic fragmentation is examined by following changes in pH during digestion of CIg and then calculating the number of bonds cleaved. Sequential samples are examined on SDS-polyacrylamide gel electrophoresis.

### Honors and Awards:

None

Publications:

1. Kessler, C.M., Bell, W.R.: Regulation of Fibrinogen Biosynthesis: Effect of Fibrin Degradation Products, Low-Molecular-Weight-Peptides of Fibrinogenolysis and Fibrinopeptides A and B. J. Lab. Clin. Med. 93: 758-767, 1979.

2. Kessler, C.M., Bell, W.R.: The Effect of Homologous Thrombin and Fibrinogen Degradation Products on Fibrinogen Synthesis in Rabbits. J. Lab. Clin. Med. 93:768-782, 1979.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF **INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10051 01 CP |

PERIOD COVERED

October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Platelet Membrane Potential Changes

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Bruce Seligman | Research Fellow, LCI, | NIAID |

COOPERATING UNITS (if any)

Laboratory of Clinical Investigation, NIAID

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.1 | 0.1 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Fluorescenated cyanine dyes when localized in biological membranes will fluoresce in response to a transmembrane electrical potential change. Recently researchers have demonstrated that the membrane potential of human platelets change in response to stimuli such as ADP and thrombin. Our current project is exploring the basics of this technique and the possibility of using this technique to assess platelet function through clinically relevant responses to various physiological and pharmacological stimuli. Basic questions relating to the mechanism of action of these various agents may also be answered.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10051 01 CP

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Platelet Membrane Potential Changes
Previous Serial No. None

Principal Investigator: Dr. Jerome A. Donlon

Other Investigator: Dr. Bruce Seligman

Man Years:

| | |
|---|---|
| Total | 0.1 |
| Professional: | 0.1 |
| Other: | |

## Project Description

### Objectives:

1. Determine optimal preparation and suspension conditions for platelets to give reproducible responses to ADP, thrombin and epinephrine.

2. Evaluate platelet membrane potential response in the presence of various agents (e.g., aspirin, persantin, urea, platelet antibodies, fibrinogen, factor VIII).

3. Evaluate platelet membrane response of abnormally functioning platelets. (Bernard Soulier, storage pool disease).

4. Correlate membrane potential changes with aggregation phenomena or release phenomena. Role of calcium and phospholipids.

### Methods Employed:

Human platelets prepared by low speed centrifugation or gel filtration. Fluoresceinated cyanine dye, measured by a fluorescence spectrophotometer.

### Major Findings

Although a sensitive transmembrane potential response was noted to ADP and thrombin, the response was variable. This variability may be related to platelet preparation, buffer, cations or plasma proteins.

### Projection:

Optimal platelet preparation procedures, buffers and cations for reproducible, meaningful responses will be determined. Membrane response to aggregating agents, antibodies, coagulation factors, aspirin and drugs.

Honors and Awards:

None

Publications:

None

SMITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
**INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER
Z01 CL 10052 01 CP

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

Platelet Membrane Glycoprotein Study

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CP | CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 0.10 | PROFESSIONAL: 0.08 | OTHER: 0.02 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

At least three major glycoproteins of human platelet membranes have been defined, purified and characterized. One glycoprotein (GPI) which is absent from the surface of Bernard-Soulier platelets also may be associated with the ristocetin receptor. Our current project proposes to purify sufficient quantities of each of these glycoproteins to allow immuniziation of rabbits or goats and thereby obtain specific antiserum for each glycoprotein. These antisera would then be used to evaluate the presence of each glycoprotein on platelets from patients with thrombosis or bleeding problems. In addition, the antisera can be used to probe the receptor function of each glycoprotein. The study will prepare glycoproteins from the platelets of normal human volunteer donors.

Project No. Z01 CL 10052 01

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Project Title: Platelet Membrane Glycoprotein Study
Previous Serial No.: None
Principal Investigator: Dr. Jerome A. Donlon

Other Investigators: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total | 0.10 |
| Professional: | 0.08 |
| Other: | 0.02 |

## Project Description

Objectives:

1. Prepare significant quantities of normal human platelet membrane glycoproteins.

2. Obtain specific antiserum to each of the purified glycoproteins.

Methods Employed:

1. Preparation of washed intact platelets by repeated low speed centrifugation.

2. Preparation of platelet membranes by osmotic lysis and ultracentrifugation.

3. Detergent or 3M salt extraction of membrane glycoproteins.

4. SDS-polyacrylamide gel electrophoresis.

5. Column chromatographic separation by molecular weight.

6. Alternatively, lectin affinity chromatography.

7. Standard immunization procedures with purified GP and appropriate IgG isolation and absorption.

Major Findings:

A prototype run using the platelets from 30 ml of whole blood demonstrates the three GP bands on SDS polyacrylamide gel electrophoresis. This amount of material is insufficient for immunizations, although representing a good yield from the original platelets.

Projections:

1. Extend the preparation to platelet concentrates representing platelets from 500 to 1000 ml of whole blood.

2. Explore various solubilization procedures and detergents, to selectively elute glycoproteins (e.g., preparations that are used to isolate HL-A antigens).

3. Use various lectin affinity columns to minimize preparation time and handling and to selectively isolate glycoproteins.

Honors and Awards:

None

Publications:

None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10053 01 CP |

PERIOD COVERED
October 1, 1978 thru September 30, 1979

TITLE OF PROJECT (80 characters or less)

Determination of lactate dehydrogenase isoenzymes for the detection of complications after cardiac operations.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

1. Dr. N.M. Papadopoulos, CC, CPD, Research Biochemist, Principle Investigator

2. Dr. C. Hufnagel, Chairman, Dept. of Surgery, Georgetown University Medical Center.

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Md. 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.45 | 0.25 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Our technique of electrophoretic determination of lactate dehydrogenase (LD) isoenzymes has been improved by: 1) clear separation and demonstration of the isoenzymes on agarose gel covered slides which allowed accurate quantitation 2) use of the same method to obtain normal patterns in tissues and blood cells, as well as reference values in serum for meaningful comparisons and correlations of results and 3) estimation of the ratio of the cardiac associated LD-isoenzymes-1 and 2. The improved technique enhanced diagnostic discrimination of myocardial infarction and other complications in patients undergoing cardiac operations.

Project No. Z01 CL 10053-01 CP
1. Clinical Center, Clin. Path. Dept.
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial No.: None

Principal Investigator: Dr. Nicholas M. Papadopoulos

Other Investigator: Dr. Charles Hufnagel

| | | |
|---|---|---|
| Man Years: | Total: | 2.2 |
| | Professional: | 2.0 |
| | Other: | 0.2 |

## Project Description

### Objectives

To enhance the accuracy of lab tests and the clinical usefulness of test results for the purpose of improving health care service.

1) By increasing the sensitivity and specificity, and improving the reliability of the electrophoretic method for the determination of LD-isoenzymes.

2) By conducting clinical research to associate changes of LD-isoenzyme patterns with defined pathological conditions and the clinical course of disease. This forms the basis for the interpretation of tests results and their association with clinical conditions.

### Method Employed

Electrophoretic fractionation of LD-isoenzymes. Quantitative determination by densitometry. Estimation of the ratio LD-1/LD-2.

### Major Findings

Determination of LD-isoenzymes and estimation of the ratio; LD1/LD2, has emerged as a new biochemical index in the diagnosis of myocardial infarction. The accuracy and reliability of our test has been established by:

1) The concept that test results are more meaningful when associated with the clinical events, as pointed out in a recent report (1).

2) Detection of myocardial infarction in patients undergoing cardiac operations (2).

3) Detection of complications in patients undergoing cardiac operations (3).

## Significance

The improvement of the method for the electrophoretic determination of the LD-isoenzymes and the new experience gained from its clinical application enhanced the reliability and diagnostic discrimination.

## Proposed Course

1) Application of the test to provide useful information to the physicians of the Clinical Center.

2) Application of the test in studies of human disease to obtain new information for the advancement of biomedical knowledge.

## Publications

1) Papadopoulos, N.: Improving reliability of the ratio LD-1/LD in the Diagnosis of myocardial infarction. Clin. Chem. 25, 1185. 1979,

2) Papadopoulos, N. and Hufnagel, C.: Evaluation of lactate dehydrogenase isoenzyme patterns in serum of patients undergoing cardiac surgery. J. of Thor. and Cardv. Surgery 76, 173-177. 1978.

3) Papadopoulos, N. and Hufnagel, C.: Detection of complications in cardiac operations by lactate dehydrogenase isoenzymes. Clin Chem. 25, 1085. 1979.

| | | |
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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10054 01 CP |

PERIOD COVERED
October 1, 1978 thru September 30, 1979

TITLE OF PROJECT (80 characters or less)

Electrophoretic Determination of Serum Lipoproteins.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Dr. N.M. Papadopoulos, Research Biochemist, Principle Investigator

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTIO.
Clinical Chemistry Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Md. 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.55 | 0.25 | 0.3 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A sensitive electrophoretic test system for the determination of lipoproteins has been improved and applied in the study of hyperlipidemias. The refinement of the original technique together with the new information gained by its application, enabled improvement of identification and expansion of the classification system of the lipoproteinemia phenotypes into 2 normolipidemic and 6 hyperlipidemic types (1).

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10054-01 CP
1. Clinical Center, Clinical Pathology
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through September 30, 1979

Previous Serial No.: None

Principal Investigator: Dr. Nicholas M. Papadopoulos

Other Investigator: Mr. D. Everett

| | | |
|---|---|---|
| Man Years: | Total: | 0.55 |
| | Professional: | 0.25 |
| | Other: | 0.3 |

## Project Description

### Objectives

To enhance the accuracy of lab tests and the clinical usefulness of test results for the purpose of improving health care lab service.

1) By improving the electrophoretic method used for the determination of serum lipoproteins.
2) By application of the method in clinical investigations to changes of normal lipoprotein electrophoretic patterns with defined pathological conditions. This forms the basis for the interpretation of test results and their association with clinical conditions.

### Methods Employed

Fractionation of serum lipoproteins by agarose gel electrophoresis; application of the test for the determination of lipoprotein patterns in normal subjects and hyperlipoproteinemia phenotypes.

### Major Findings

The application of the improved agarose gel electrophoretic system for the determination of lipoproteins in serum samples from normal subjects and patients resulted in the following new information:

1) Update of the lipoprotein phenotyping system (1)
2) Determination of abnormal lipoprotein patterns in the serum of patients and their association with defined pathological

conditions. All these patterns form a reference record for the diagnosis and evaluation of lipoprotein abnormalities in normal subjects and patients. They provide useful information for appropriate treatment with established therapeutic measures.

## Significance

The detection of lipoprotein abnormalities aids the early intervention by therapeutic measures for the prevention of cardiovascular diseases. The sensitive electrophoretic test system employed accomplishes this purpose.

## Proposed Course

Continued application of the lipoprotein electrophoretic test system for the following purposes:

1) To detect lipoprotein abnormalities characterized by the presence of extra lipoprotein bands or the absence of lipoprotein fractions in serum, and their association with clinical conditions.

2) The study of the role of lipoproteins in the pathogenesis of atherosclerosis.

## Publications

1) Papadopoulos, N.: Hyperlipoproteinemia phenotype determination by agarose gel electrophoresis updated. Clin. Chem. 24, 227. 1978.

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PHARMACY

DIAG. RADIOL.

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## DIAGNOSTIC RADIOLOGY DEPARTMENT

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October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## DIAGNOSTIC RADIOLOGY DEPARTMENT

### DEPARTMENTAL MISSIONS AND GOALS

Provision of the most modern and comprehensive diagnostic radiologic service to the Clinical Center patients remains the prime objective of the Diagnostic Radiology Department. In our attempts to obtain this objective, particular attention was directed to the following general goals during the past year:

1) The recruitment and retention of a competent medical staff.

This is perhaps the most important of all secondary departmental objectives. As federal physicians' salaries become less and less competitive we must provide a uniquely stimulating and intellectually challenging environment to attract new staff members.

2) The stimulation of departmental research activity.

Active programs of independent and collaborative research have been successful in several ways. Such programs attract ambitious and innovative young radiologists thus strengthening the professional staff. They also contribute to a general improvement in patient care by demonstrating to the hospital's clinical staff the value of new radiologic techniques. Significant improvement in the effective therapy of some endocrinologic diseases has resulted from research done here in selective venous sampling for accurate localization of endocrinologic disease and from superselective vaso-occlusive techniques for the treatment of some types of endocrinologic malfunction.

3) The improvement of professional education for radiologists and technicians.

A fairly rapid turnover in physician personnel requires a continuing effort to maintain adequate levels of departmental expertise in all areas of radiologic subspecialty. Foreseeing the loss of Dr. X, expert in subspecialty Y, requires that Dr. Z be trained in that subspecialty so as to prevent major holes in Department coverage. The recent introduction of ultrasound and CT has called for major training efforts for departmental physicians and technicians alike.

4) The encouragement of interdepartmental clinical and teaching conferences.

It is only by our instructing the clinical staff on what diagnostic radiology can and should do that the clinical use of radiologic examinations can be properly tailored to meet individual patient's needs.

5) The improvement of departmental responsiveness to changing Clinical Center needs.

It has been obvious for some time that radiologic services to the physicians of the Outpatient Department were deficient. Our opening, recently, of the satellite outpatient x-ray facility will improve the quality of such service.

6) The careful control and minimization of X-ray exposure to patients and staff. In conformity with the President's directive about radiation exposure levels, increasing attention is being placed on radiographic techniques, film-screen combinations, collimation and more frequent checks by our physicist of equipment safety. The recommendations of the National Conference on Referral Criteria for X-ray Evaluations have caused us to be even more aware of the role we should be playing in the study of techniques to maximize diagnostic yield and minimize radiation exposure of patients.

7) The improvement of the efficiency, responsiveness and morale of the Department's administrative staff.

Recent changes in administrative personnel and duty assignments have met with early success in all of the above regards. Further improvements are expected to result from minor modifications and clarification of individual responsibility.

## DEPARTMENTAL ACTIVITIES

Both the number of conventional X-rays taken and the total number of diagnostic examinations performed increased in comparison to last year (5% and 6% respectively). The trend, noted in the past, of a disproportionately large increase in examinations which are expensive in terms of time, personnel, and equipment was again observed. In the past year we have seen increases of 17% in the number of special procedures, 10% in the number of CT examinations (a 49% increase in body scans and a 10% decrease in head scans - vide infra) and a 20% increase in examinations performed in the animal research area. (See table of departmental activity, DR-9).

### Computed Tomography

Although clinicians have been slow to accept CT scanning techniques, the situation has changed dramatically in the past several years, and we now note a tendency to regard CT as a diagnostic panacea. The 49% increase in the number of body scans in the past year is a reflection of the diagnostic contributions made by the technique. It also represents a percentage increase higher than we thought we could obtain; however, our saturation point using the available scanning equipment has been reached. As we anticipated in last year's annual report, the number of head scans performed has decreased (10%). The decrease is not as profound as we had expected when we discontinued providing routine diagnostic scanning for WRAMC and USNMC and probably represents a rough future baseline for head scanning at the Clinical Center unless or until there is further change in Clinical Center patient mix.

We have ordered a high speed universal scanning unit because the number of Institute patient protocols requiring single or sequential body scans continue to increase and we cannot accomodate a significantly larger number of patients on our current scanner. The dedicated head scanner now in the Department will be replaced by this universal unit which will permit us to perform the head scans demanded of us and permit us to increase our capacity for body scanning. The coordination of room rennovation and installation of the new scanner with continuing patient demands poses a problem of which we are aware.

During the year we have further improved the CT body scanner by installing a high resolution mode which will permit better demonstration of minor variations in tissue densities and of fine anatomic detail. A significant improvement in the efficiency of the scanner resulted from software modifications which allow more rapid computer processing of scanning images.

A major portion of the research activity of the Diagnostic Radiology Department derives from the CT body scanner. Nineteen papers based primarily or in part on CT techniques have been published during the past year. Our Development of a new technique to improve detection of hepatic metastases has progressed from laboratory and animal studies to clinical trial. Preliminary clinical data (to be presented at the Radiological Society of North America this fall) warrants continuing enthusiasm. Papers reporting the usefulness of CT in the study of patients with cancer have been or are being written - the studies include data derived from patients suffering from carcinoma of the ovary, testicle, pancreas, colon, lung, and adrenals. The contributions of CT to the study of the lymphomas, assorted endocrine tumors, lesions of soft tissues and bone are under active investigation.

The CT Section has become a major attraction for visitors; in the past year we have hosted scientists and dignitaries from North and South America, Europe, Asia, Africa, and Australia. While some of the visits have been more or less perfunctory, others have permitted in depth discussion of CT techniques.

Recognizing the revolutionary diagnostic impact of CT scanning, the Department has arranged to sponsor an area-wide CT meeting on a bi-monthly schedule. We expect the enthusiastic participation of radiologists from the Baltimore-Washington area with whom we can share our experience and from whom we hope to learn about the application of CT in disease states not seen at the Clinical Center. Approval of CME credit for this meeting is anticipated.

The two departmental scanners require two full-time radiologists, four technicians, one appointment file clerk, and the part-time efforts of our physicist. Maintanence contract costs were $65,213 this year, representing an increase of $4145 (7%) over last year. Tube replacement costs were $4864 in 1978 and $6158 in 1979 (an increase of 26%).

Ultrasound

The number of patients seen has not increased significantly. We presently seem to be meeting the Clinical Center's needs adequately in this Section. However, the Ultrasound section cannot increase its patient load any further because of the severe limitations on space and personnel as mentioned in last year's annual report. Average scheduling time runs from three to five days with flexibility possible to permit the addition of urgent cases as the need arises.

Our research interest continues to be extensive and active. The Varison-sonochromascope is operational and in clinical use. This unit was designed and built by the National Bureau of Standards through an NIH grant and has allowed us to expand our diagnostic capabilities to quantitatively evaluate diffuse organ disease. In addition, we are clinically testing another new type of scanner designed with Clinical Center funding, a static scanner annular array. This unit was designed to improve the ultrasound beam lateral resolution.

We have recently completed a 10 month study of the ultrasonic evaluation of the biliary system in monkeys with surgically obstructed common bile ducts. Results of this study, plus the results of our work on computer analysis of the pancreas in patients with cystic fibrosis, will be presented at the annual national meeting of the American Institute of Ultrasound in Medicine in August of 1979. An exhibit entitled "Ultrasound Evaluation of Testicular Tumors" won first prize at the annual meeting of the American Urological Association in May 1979.

We are also involved with the National Institute of Arthritis, Metabolism and Digestive Diseases and the National Center for Health Statistics in designing an ultrasound screening program for the diagnosis of gallbladder disease.

With the recent installation of computer tape drive to the intradata computer in the Ultrasound Section we expect in the next year to begin to investigate the role of ultrasound in radiation therapy planning. In conjunction with investigators from the Division of Computer Research and Technology we also hope to begin computer manipulation of the ultrasound image.

In June 1979 we cosponsored with the National Bureau of Standards the Fourth International Symposium on Ultrasonic Imaging and Tissue Characterization. During this week-long meeting we presented our early clinical results on obtaining ultrasound pancreatic tissue signatures. For the past several months in conjunction with the Physical Therapy Department and Engineering Department of the Clinical Center we have investigated the role of ultrasound in evaluating tongue movements in normal and diseased patients. The preliminary results of this study are to be presented at the national meeting of the American Association of Physical Medicine in November of 1979.

We continue to be involved extensively in several clinical research protocols within the Clinical Center. Our work on Burkitt's lymphoma has been completed and published and shows the usefulness of ultrasound in evaluating that disease. We are also engaged in a clinical trial comparing various imaging systems for the diagnosis of hepatic metastases and in an investigation of the role of ultrasound in staging esophageal cancer.

The Ultrasonic Section of the Department of Diagnostic Radiology requires two full-time radiologists, two technicians and an appointment file clerk. Maintenance costs approximate $6000/yr.

There has been no increase in the size of the professional or technical staff during the past several years during which we have developed the CT and Ultrasonic Sections of the Department. These Sections generated 6700 examinations during the past year.

## Special X-Ray Procedures

An increase of 17% in the number of special procedures was observed this year. Concomitant with this increase is the further increase in the hours devoted to the performance of these procedures. An ever larger proportion of special procedures entail multiple selective and superselective catheterizations. Whereas several years ago inferior vena cavography (requiring about 20 minutes for satisfactory performance) represented a high percentage of the total number of special procedures, in 1979 parathyroid venous samplings or interventional radiographic studies have become far more numerous. The latter sophisticated techniques may require the presence of several radiologists as well as several technicians and nurses and may last for a number of hours. Perhaps a better way for us to record the impact of the special procedures on the Department would be to record the time spent in their performance rather than in a mere enumeration of studies performed.

Last year's annual report noted the long term trend of decreasing numbers of conventional neuroradiologic procedures performed by the Diagnostic Radiology Department. The following chart documents the profound change in departmental neuroradiologic activity since the introduction of CT and concomitant with the fall-off in the numbers of neurosurgical cases seen by the NINCDS.

| Dates | Head CT | Cerebral Angiography | Pneumo-encephalography |
|---|---|---|---|
| 7/1/74 - 6/30/75 | -- | 135 | 52 |
| 7/1/75 - 6/30/76 | 1877 | 94 | 13 |
| 7/1/76 - 6/30/77 | 2750 | 67 | 9 |
| 7/1/77 - 6/30/78 | 2936 | 72 | 6 |
| 7/1/78 - 6/30/79 | 2655 | 32 | 2 |

The chart dramatizes a fact which may place an extraordinary strain on the Department and have a marked effect on our staffing needs. Note that in 74-75 we performed a total of 187 neuroradiologic studies while in 78-79 the number totalled 2689. If the new neurosurgical staff anticipates a significant increase in the demand for conventional neuroradiologic special procedures, we may have difficulty fulfilling their needs equipped and staffed as we are.

## Research Facility

The number of animal studies performed in the research facility this year increased 20%. Active projects involving the development of new catheter materials and catheterization techniques continue. Studies to improve our ability to direct the catheter tip into vessels heretofore inacessible show promise as do our efforts to improve balloon catheters and materials for vascular occlusion. The results of animal studies of iatrogenic obstruction

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of the biliary tree are to be presented at the annual meeting of the American Institute of Ultrasound in Medicine. We have begun clinical studies of an agent to opacify the liver following the accumulation of satisfactory data from our ongoing animal experiments.

Two full-time technical personnel work with members of the professional staff to maintain the research facility.

## Teaching and Education

Our teaching and educational conferences have been so well received that we are unable to meet the requests for further increases in the number of such activities. We average more than two interdepartmental conferences each day. Members of the staff continue to give teaching sessions at D.C. General Hospital, USNMC, GWU Hospital and the AFIP. Students from the USUHS third year class are rotating through our Department on a regular basis for clinical experience. Preliminary discussions with the Chief of Radiology of the USUHS have begun about the extent and nature of our cooperative teaching efforts. I anticipate that several members of the AFIP and USUHS staffs will participate in joint programs at the Clinical Center and that several members of our staff will be given academic titles for their participation in the teaching program at the USUHS. A plan for rotating additional USUHS students thru the Diagnostic Radiology Department is being discussed. This Department will keep the Director of the Clinical Center fully informed as these plans develop.

## Department Coverage After Normal Working Hours.

The institution of 24 hour in-house technician coverage has proven very successful, permitting more rapid delivery of x-ray services and allowing a significant savings in overtime costs (approximately 40%).

## Plans for ACRF

A major effort demanding increasing amounts of time is required to plan for purchases and personnel for the new Department. A tightly arranged schedule for equipment acquisition and for necessary increases in personnel is being developed so as to conform to the budgetary restrictions placed on us by the Clinical Center. A preliminary estimate of dollar requirements reveals a shocking figure. In order to equip the new Department with the machinary necessary for its satisfactory initial operation we will need funding for capital equipment of about $6,000,000. We have been told that equipment to be installed in the Department by opening day should be on campus by May 1981. That means, of course, that $6,000,000 must be committed from the FY 1980 and 1981 budgets, since we require a lead time of 9-12 months for most purchases. Since our preliminary estimate, made 18 months ago, equipment costs have soared by about 30%.

## Capital Equipment Acquisition for Existing Department

For the past three years we have postponed the purchase of all but the most essential equipment. Profound technologic improvements and continuing physician demand for those examinations made possible by the most modern equipment have influenced our decision to purchase new ultrasound and universal CT scanning units this year. We anticipate that both of these machines will be moved into the ACRF. In the coming year we will request approximately $150,000 for necessary improvements to the CT scanner and will suggest that we purchase a new pluridirectional tomographic unit. (Approximate cost $285,000) This latter unit will replace the Phillips Polytome which was purchased in 1968 and which represents the least versatile and most underutilized piece of equipment in the Department. Routine large part tomography, for which clinical demand is now great and will increase, cannot adequately be performed by the Polytome, and its use is therefore limited to the performance of about 8 patient examinations per month. Replacement of the Polytome with the much more modern and versatile Statamatix, which is capable of doing routine filming as well as all uni- and polydirectional film tomography, is most emphatically recommended. The unit can be safely and easily moved to the ACRF, and in the meanwhile will fulfill growing departmental needs for the next 18-24 months.

## MAJOR PROJECTS AND RESEARCH

Listed below are the major research projects now under investigation in the Department. The appended description of the projects are adequate and require no summation. (See Project Reports, pp DR-11 - DR-22).

1. Evaluation of CT Body Scanning in Oncologic Patients.
2. IV Hepatosplenography.
3. Evaluation of Contrast Agents for Transcatheter Organ Ablation.
4. Evaluation of Serial Hepatic Scans in Patients With Primary and Secondary Hemochromatosis Using Computed Tomography and Ultrasound.
5. Development of Opaque Agent for Opacification of the Liver on Computer Tomography.
6. Lymphography in Oncologic Patients.

## PROBLEMS

### Physician Recruitment and Retention

As the sine qua non of any hospital department is its professional staff, I shall direct a major effort to the recruitment of competent medical staff. This requires a major effort because of the inequities, and present Federal salary schedules for radiologists. Last year for example one radiologist was paid $325,000 on contract by one Federal medical installation. The peculiarities of the Federal pay scale permit a junior member of my staff who is paid about $600/week to be offered $600/day to provide radiologic services to the above mentioned Federal facility. In the past, NIH radiology has had to compete against private practice salaries (we could not), against academic salaries (we had a fighting chance) and against other Federal salaries (we offered equal income and more rewarding professional environment) - so we did well. However, when the major Federal medical research center can offer an income only 10-25% of that offered by a small DOD medical facility, our chances of retaining staff become smaller.

I must again emphasize that in the face of such competition we must have funding adequate to maintain a stimulating clinical and research environment. Funds for meetings and continuing education must be generous, and rather than facing further cuts, they should be increased. Progressive loss of these fringe benefits will make an already difficult staffing problem an absolutely impossible one.

### Clerical Staffing

While not as dramatic, another staffing problem of major importance is that which arises from the shortage of competent stenographic and clerical personnel. During several periods in the past year there has been a 4-5 day delay between the dictation of film reports and their being typed. Our secretarial pool is adequate, but a resignation or two could again precipitate a very serious problem.

### Space

In previous annual reports I have bemoaned the inadequacy of space in the Diagnostic Radiology Department - space for comfortable patient waiting areas, space for physicians' offices, space for the ultrasonic suites and space for the animal research facility. Those serious deficiencies previously decried persist, but when we move into the new Department in 18-24 months they will be remedied. Until then we will be patient.

## SUMMARY OF DEPARTMENT ACTIVITIES

| | 7/1/77-6/30/78 | 7/1/78-6/30/79 | % Change |
|---|---|---|---|
| #MDs | 13 | 12-13 | 0 to -8% |
| #Technicians | 26 | 24-26 | 0 |
| #Other Staff | 26 | 26 | 0 |
| #X-Ray Exams | 47284 | 48167 | +5% |
| #Department Diagnostic Exams | 53746 | 56521 | +6% |
| #Specials | 713 | 869 | +17% |
| #CT Head | 2750 | 2655 | -10% |
| #CT Body | 704 | 2297 | +49% |
| #Ultrasound Exams | 1560 | 1728 | +1% |
| #Animal Research Exams | 735 | 805 | +20% |
| #Publications | 52 | 68 | +30% |

A number of papers listed, i.e. some of those authored by Dr. Long and all authored by Dr. Margulis are based on work started elsewhere but completed after Dr. Long joined our staff. We can thus predict a significant decrease in the number of papers that we will report in next year's Annual Report.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 04006-02-DR |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

EVALUATION OF CT BODY SCANNING IN ONCOLOGIC PATIENTS

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | | |
|---|---|---|---|---|
| PI | Dr. N.Reed Dunnick | Staff Radiologist | DRD | CC |
| OTHER | Dr. Thomas Shawker | Staff Radiologist | DRD | CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

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| TOTAL MANYEARS:<br>1 | PROFESSIONAL:<br>2 | OTHER:<br>2 |

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

### Objectives

Comparison of CT scanning with other imaging modalities in the detection and follow-up of tumors. To extend our ability to image malignancies at presentation for staging purposes as well as to demonstrate followable disease.

### Methods Employed

CT is performed as a staging modality as well as at periodic follow-up intervals. Currently, patients with malignant lymphomas, ovarian carcinoma, malignant melanoma, testicular tumors, adrenal carcinomas, prostate carcinoma, oat cell carcinoma of the lung, and a variety of soft tissue sarcomas are being most intensively studied.

## Major Findings

Upper abdominal CT scans were performed on 45 consecutive patients with biopsy proven, previously untreated small cell carcinoma of the lung. Evidence of metastases was found in 16 (36%) patients. The most common site of metastases was the liver (27%); CT had a sensitivity of 88% specificity of 94% as compared with biopsy results. Evidence of retroperitoneal metastases was found in 7 (16%) patients.

Intravenous extension of endocrine tumors is now much better appreciated. This radiographic diagnosis can frequently be made by CT.

The installation of dialysate mixed with water soluble contrast material into the intra-peritoneal space has resulted in significantly improved anatomic definition of the peritoneal cavity. In some patients, tumor defects can be appreciated studying the peritoneal surface.

## Publications

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 04011-02-DR |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

IV HEPATOSPLENOGRAPHY

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | | |
|---|---|---|---|---|
| PI | Dr. M. Vermess | Associate Chief | DRD | CC |
| OTHERS | Dr. R.N. Adamson | Chief | LCHPH | NCI |
| | Dr. J.L. Doppman | Chief | DRD | CC |
| | Dr. Dulal Chatterji | | PHAR | CC |
| | George Grimes | | PHAR | CC |
| | Mary Girton | R.T. | DRD | CC |

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Vienna, VA 22180

LAB/BRANCH
Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

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☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Results and Current Objectives

Last year we made a very significant step forward. We have obtained permission from the FDA to start Phase I Clinical Trials with the contrast material which was developed in this project: Ethiodized Oil Emulsion 13 (EOE 13). Ten patients were injected and significant improvement in the visualization of the spleen and liver was obtained. A report is being prepared for the FDA concerning the ten injected patients with the request to continue trials on a broader patient base.

Concerning current objectives in further laboratory work, we are studying the metabolic routes of this contrast material. Also we are trying to establish an optimal time for the CT scan of liver and spleen, that is, when the highest concentration of the contrast material is present in the liver and spleen. In addition, we plan to use Iodine$^{131}$ labeled contrast material in order to follow the excretion and elimination of the contrast material from the body.

## Methods

The experiments outlined in the objectives are conducted on rats and healthy Rhesus monkeys with the increased opacity of the spleen and the liver measured by CT scans following the intravenous infusion of EOE 13. The clearance of the contrast material from the liver and spleen is determined by short-term follow-up scans.

A second group of experiments is conducted on Rhesus monkeys with induced hepatic cell carcinoma to determine the optimal increase in opacity of the liver to detect small hepatic lesions and improve the diagnosis of hepatic metastases.

## Major Findings

It was demonstrated that intravenously injected Ethiodol emulsion with approximately 60% of the particles between 2 and 4 microns in diameter will accumulate in the liver and spleen, significantly increasing opacity. Furthermore, it was demonstrated that the tumors involving the liver do not accumulate this contrast material thereby increasing the density differential between normal and abnormal tissues which greatly facilitates x-ray diagnosis.

## Significance of Research

A new intravenous contrast material was developed (with the utilization of previous French experimental clinical work) which on intravenous injection opacifies the liver and spleen. The contrast material developed in this project is currently undergoing Clinical Phase I Trials.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 04013-01-DR |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

EVALUATION OF CONTRAST AGENTS FOR TRANSCATHETER ORGAN ABLATION

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

|  |  |  |  |  |
|---|---|---|---|---|
| PI | Dr. J.L. Doppman | Chief | DRD | CC |
|  | Mary Girton | R.T. | DRD | CC |
| OTHERS | Richard Diggs | Technician | DRD | CC |
|  | Mark Popovsky, M.D. | Pathologist | Pathology | NCI |

COOPERATING UNITS (if any)

LAB/BRANCH
Diagnostic Radiology Department

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☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

To evaluate currently used radiopaque agents in a wedge catheter system as a means of achieving parenchymal damage in a variety of endocrine tumors.

Methods Employed

Prolonged staining of parathyroid adenomas following injection of moderate doses of contrast material through a wedge catheter system has led to permanent control of hyperparathyroidism in a small number of clinical subjects. We are investigating in laboratory animals the potential for using this wedge catheter system to permanently ablate organ function without the use of particulate embolizing agents or plastics.

Balloon catheters are used to obstruct arteries into which undiluted contrast material is perfused into the vascular bed of the target organ. Currently kidneys in a variety of animals are being so treated in an attempt to produce medical nephrectomy without the risk of embolization. Organs so perfused remain stained for several hours, and absence of urine production in follow-ups ranging 6 to 8 weeks have been demonstrated. Currently under investigation is the need to obstruct arterial inflow following such stainings and the long term results of such interventions.

## Significance of Research

The ability to ablate function of highly specialized tissues, endocrine adenomas, kidneys without using particulate or non-biodegradable embolizing agents would have significant application. For this reason the use of hypertonic contrast media in a wedge system to produce acute cellular damage is being investigated.

## Publications

Doppman JL, Brown EM, Brennan MF, Spiegel A, Marx SJ and Aurbach GD: Angiographic Ablation of Parathyroid Adenomas. Radiology 130:577-582, March 1979

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 04014-01-DR |

PERIOD COVERED

October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

EVALUATION OF SERIAL HEPATIC SCANS IN PATIENTS WITH PRIMARY AND SECONDARY HEMOCHROMATOSIS USING COMPUTED TOMOGRAPHY AND ULTRASOUND

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | | |
|---|---|---|---|---|
| PI | Dr. J.L. Doppman | Chief | DRD | CC |
| | Dr. A.W. Nienhuis | Chief | H | NHLBI |
| | Dr. J.A. Long | Staff Radiologist | DRD | CC |

COOPERATING UNITS (if any)

LAB/BRANCH

Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

To determine whether absorption coefficients of the livers of patients with secondary hemochromatosis, when measured serially, can indicate increasing or decreasing iron loads when such patients are undergoing chelation therapy.

Methods Employed

Secondary hemochromatosis with its effects on the liver and heart is the principal cause of death currently in patients with thalassemia and other congenital anemias. Use of long term therapy with chelating agents attempts to decrease this iron load in these subjects. Critical to the evaluation of this therapeutic trial is the total iron body load, previously measured by serial hepatic biopsies. Computerized tomography of the liver provided absorption coefficients in patients with excessive iron stores, an average absorption coefficient far above the normal liver. A study of normal livers had revealed

PHS-6040
(Rev. 10-76)

absorption coefficients ranging from 10 to 25 EMI units, whereas livers with excessive iron loads have generally had absorption coefficients above 35. A group of patients with secondary hemochromatosis undergoing long term chelation therapy are being serially scanned to determine whether decreases in liver iron are reflected by decreases in absorption coefficients as measured on CT studies. These findings will also be related to ultrasonographic indications of increased collagen deposition using computer generated tissue measurements and then correlating each finding with available liver biopsies.

## Significance of Research

Determining the iron load of patients undergoing multiple transfusions for congenital anemias and following the response to chelation therapy are important clinical services, perhaps replacing the serial liver biopsy which is not without risk. The follow-up has been too short for significant results. However, multiple otherwise unappreciated CT observations have been made that help confirm the diagnosis of hemochromatosis and show iron deposition in endocrine organs and extramedullary hemochromatosis.

## Publications

Mills SR, Doppman JL and Nienhuis AW: Computed tomography in the diagnosis of disorders of excessive iron storage of the liver. J Comput Assist Tomogr 1:101-104, 1977

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 04015-01-DR |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
DEVELOPMENT OF OPAQUE AGENT FOR OPACIFICATION OF THE LIVER ON COMPUTER TOMOGRAPHY

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | | |
|---|---|---|---|---|
| PI | Dr. M. Vermess | Associate Chief | DRD | CC |
| | Dr. J.L. Doppman | Chief | DRD | CC |
| OTHERS | Mary Girton | R.T. | DRD | CC |
| | Richard Diggs | Technician | DRD | CC |

COOPERATING UNITS (if any)
Outside NIH: B. Halpern, Ph.D., Polysciences, Inc., Warrington, PA
Research Associate

LAB/BRANCH
Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER
☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

## Objectives

To determine optimal particle size for a colloidal suspension to be used for increasing absorption coefficients of the liver and facilitate the detection of small hepatic metastases.

## Methods Used

We have received from Polysciences, Inc., latex particle suspensions ranging in diameter from 0.5 to 5 microns. These are labeled with fluorescent dyes to enable quantitation of tissue distribution following intravenous injection of laboratory animals. We are currently experimenting with the extraction of these labeled latex particles from animal tissues for quantitative measurements. The extraction and exact quantitation of these particles presented unexpected difficulties and we are exploring alternate ways for this purpose. When these problems are solved, the optimal particle size for hepatic deposition will be determined. This will be followed by injection of biodegradable particles (contrast materials) which will be prepared and tested in animals seeking a suitable opaque agent for hepatic CT scanning.

## Significance of Research

We are trying to demonstrate that certain organs preferentially take up intravenously injected particles of specific diameters. This would prove to be a significant help in the development of an ideal intravenous contrast material for the opacification of the liver and spleen and may facilitate earlier detection of small liver metastases on computerized tomographic examinations of the liver and spleen.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04016-01-DR |

PERIOD COVERED October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)

LYMPHOGRAPHY IN ONCOLOGIC PATIENTS

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI Dr. N. Reed Dunnick Staff Radiologist DRD CC

COOPERATING UNITS (if any)

LAB/BRANCH Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 1 | PROFESSIONAL: 1 | OTHER: 2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

To evaluate the role of lymphography in comparison with other diagnostic modalities such as ultrasound and computer tomography in the staging and follow-up of patients with appropriate malignancies.

Methods Employed

Bipedal lymphography is routinely performed on patients with a variety of malignancies, most specifically including malignant lymphomas, testicular tumors, carcinoma of the prostate, carcinoma of the ovary, and mycosis fungoides. Follow-up radiographs are performed at periodic intervals and an evaluation of the opacified retroperitoneal lymph nodes is made to assess disease progression.

PHS-6040
(Rev. 10-76)

## Major Findings

Bipedal lymphograms performed on a series of 28 patients with carcinoma of the pancreas demonstrated extrapancreatic abnormalities in 4 patients. The demonstration of extrapancreatic disease may make these patients inoperable.

A method for delivering intralymphatic contrast material to patients who have undergone previous amputations making the usual dorsal pedal lymphatic route impossible was described.

Lymphography has been useful as one of several modalities in following patients with carcinoma of the prostate. It is limited in part by the relatively poor filling of retroperitoneal lymph nodes in older patients. Bipedal lymphography has thus far been quite useful in patients with testicular carcinoma, ovarian carcinoma, and malignant lymphomas. The better detail provided by lymphography is helpful in small sites of metastatic disease. Extranodal disease is easier detected by computer tomography. Bulky disease can usually be readily identified by either method.

OCC. MED.

OPD

PHARMACY

NUCLEAR MED.

MED. REC.

FABRIC CARE

ESCD

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES

CLINICAL CENTER

ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

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PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES

CLINICAL CENTER

ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## MISSIONS AND GOALS

The primary objectives of the Environmental Sanitation Control Department during the year were to:

1. Provide the safest possible sanitary environment for the Institutes and services in the Clinical Center

2. Provide a dependable, efficient, elevator service responsive to the requirements of patients, emergencies, staff, and visitors.

3. Study the Department's manpower requirements and formalize its work and personnel procedures

4. Orient, train, and supervise its personnel so that they are proficient in carrying out the program objectives

5. Test various products and equipment in order to utilize the most modern housekeeping practices.

6. Cope with day-to-day environmental problems withing the Clinical Center and study the total environmental problems withing the Clinical Center as they relate to an institutional setting.

7. Develop an objective evaluation of the housekeeping program.

## DEPARTMENT SENIOR STAFF

Mr. John Summerour, Chief, Patient Area; Mr. John Stanmore, Chief, Day Service; Mr. Joseph Brown, Chief, Night Service Section have a combined total of ninety-six years government service, sisty-six years of this time was spent in the Environmental Sanitation Control Department.

DEPARTMENT ACTIVITIES

Employee turnover was higher than the previous year with sixty-six new employees entering on duty and forty-six leaving. Table 4 shows that 20 resigned, 1 transfered, 4 retired, 19 were terminated and 2 deceased. Individual employees and groups received 140 letters of appreciation or commendation from building tennants for services rendered.

The Department coordinated the selection, procurement, and installation of approximately 8,000 yards of carpeting during the year. This includes replacing 5,835 yards of existing carpeting. We have been able to find 6 carpet qualities within GSA Contract Schedules that meet DHEW standards.

Operator-controlled passenger elevator service was extended to 24 hour service on the D wing elevators. This was made necessary because of changing traffic patterns within the building that resulted from ACRF construction and the opening of the 10D Intensive Care Unit. We have also scheduled one housekeeping aid to assist the 10D Intensive Care Unit nursing personnel week nights from midnight to 8:30 AM (waste collection, check-outs, special elevator service)

A procedure for providing operator controlled special elevator service was also initiated in the ACRF garage. This was necessary because of frequent breakdowns with the two automatic passenger elevators.

As a result of the fire on 9 West Patient Unit, the Department used 433 hours of overtime to clean approximately 500 rooms and 2,500 pieces of furniture. Approximately 45,000 feet of wall area was also cleaned.

MAJOR PROGRESS IN RESEARCH, SERVICES, TRAINING AND DEVELOPMENT

Construction of the ACRF and building renovations continued to present the

Department with its greatest challenge. In addition to uncounted minor projects during the year, there were several major projects affecting all areas of the building. While renovations are in progress, the natural reaction is to throw in the dust towel and give up on housekeeping until conditions settle and housekeeping can be handled in a normal routine fashion.

However, renovation creates conditions which call for an actual intensification of housekeeping activities. There is a very real problem of maintenance becoming considerably more difficult, both from a psychological and a practical performance standpoint, while at the same time efficiency becomes more important.

The Department experienced major inconvenience because of constant flooding in the Clinical Center and ACRF garage. This made necessary the purchase of 4 additional 55 gallon wet-pickups.

Construction of the ACRF created many novel problems for the ESCD: areas adjacent to the construction had to be protected from contamination by the soils and waste material produced in renovation; floors became badly damaged by scratching or abrading from tracking in of particles of concrete, metal chips, splinters, mud, etc; air-bourn waste particles and dust could damage office equipment and mechanical systems. Comfort became an important factor since people react to unpleasant conditions caused by excessive dust and soil. Infection control became more difficult. The basic housekeeping principle during ACRF Construction renovation has been isolation: the remodeling work and its by-products have been completely isolated from the portion of the building not involved. Some of the more effective steps in this direction are containment barriers around the work area, mats and runners in connecting areas to entrap as much soil and dirt as possible, and restriction of sightseers walking through the area and tracking soil back into other areas.

Night Service began implementing two new work shifts to increase productivity. The first shift to begin operating was the Midnight - 8:30 AM tour; this crew was most effective during periods of freezing rain and heavy snow when clearing outside entrances and pathways leading to the Clinical Center was extremely important. This crew also assisted Clinical Center staff and visitors when their automobiles were unable to proceed because of heavy snow. The second shift, part-time 5:00 PM - 9:00 PM, was necessary to collect waste on patient areas at 7:00 PM nightly (a new procedure) and to perform check-out cleaning and other patient area emergency assignments.

The emergency assistance program for the Department operated satisfactorily during the year. Elevator operators and others were briefed several times on emergency procedures. Water pick-up equipment was renovated and replaced during the year and operated in a very satisfactory manner. The following emergencies were encountered during the year:

| | | |
|---|---|---|
| Floods: | 112 calls for | 631 staff-hours |
| Fires: | 2 calls for | 63 staff-hours |
| Electrical: | 25 calls for | 9 staff-hours |
| Others: | 24 calls for | 8 staff-hours |

Five cleaning products were evaluated: two stainless steel cleaners; two graffitti removers; one carpet spot remover; one 3M stainless steel cleaner and the carpet remover were satisfactory. The two graffitti removers were too hazardous for general use. A large carpet extractor was purchased and was used successfully to prevent carpet mildew. Three hundred and fifty new wall-mounted soap dispensers are now being tested with satisfactory results at this time.

FUTURE OBJECTIVES DIRECTED:

1. Implement new solid waste handling system based on reactivaction of existing Clinical Center trash chutes

2. Complete refresher training and certification in basic work procedures for all Department supervisors, leaders, and employees

3. Support and encourage upward mobility for employees so that they may work at their fullest potential

4. Continue to study the feasibility of phasing out manual passenger elevator service and coverting to automatic passenger elevators

5. Begin program to renovate B1B-19A and B1D-25 Locker Rooms

6. Publish new cleaning procedures in "Clinical Center Cleaning Procedure Manual," and revise 25% of programmed work plans

7. Continue to test new products and equipment

8. Coordinate selection of textiles and fabrics for draperies, furniture, and wall and floor coverings within the Clinical Center.

## TABLE 1

## ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## OCTOBER 1, 1978 through September 30, 1979

| GOVERNMENT | | STAFF HOURS | |
|---|---|---|---|
| Civil Service | | | |
| EEO Training | | 60 | |
| Employee Assistant Program | | 276 | |
| Educational Program | | 287 | |
| Adult Education | | 409 | |
| Cardiac Pluminary Resucitation | | 48 | |
| Spotlight on Safety | | 72 | |
| 2-Day Seminar on Retirement Planning | | 32 | |
| Electronics & Reading | | 6 | |
| NON-GOVERNMENT | | | |
| Upward Mobility College | | 54 | |
| | TOTAL | | 1184 |
| WITHIN DEPARTMENT | | | |
| Procedures and Orientation | | 1152 | |
| All Employee Training | | 526 | |
| | TOTAL | | 1678 |
| | GRAND TOTAL | | 2862 |

TABLE 2

## POSITIONS FILLED BY RECRUITMENT

## ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## OCTOBER 1, 1978 THROUGH SEPTEMBER 30, 1979

| MONTH | GENERAL SCHEDULE | OTHER WAGE BOARD | WG-03 | WG-02 | WG-01 | TOTAL |
|---|---|---|---|---|---|---|
| October | | | | 19 | 4 | 23 |
| November | | | | 2 | | 2 |
| December | | | | | | 0 |
| January | | | | | | 0 |
| February | | | | 4 | | 4 |
| March | | | | 6 | 2 | 8 |
| April | | 1 | | 2 | | 3 |
| May | | | | 7 | 2 | 9 |
| June | | | | 6 | 1 | 7 |
| July | | 1 | | 8 | | 9 |
| August | | | | 1 | | 1 |
| September | | | | | | 0 |
| SUB-TOTAL | | 2 | | 55 | 9 | 65 |

* Total includes 8 700-hour appointments and 53 NTE 1-year appointments

## TABLE 2

## REASONS FOR PERSONNEL LEAVING

## ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## OCTOBER 1, 1978 THROUGH SEPTEMBER 30, 1979

| RESIGNATIONS | TRANSFERS | RETIREMENTS | TERMINATIONS | DECEASED |
|---|---|---|---|---|
| Resigned when faced with possible disciplinary action<br>7 | Improve career opportunities<br>1 | Retirement disability<br>2 | Separation during probationary period<br>1 | 2 |
| To accpet non-government positions<br>6 | Transporation | Retirement optional<br>2 | Termination of temporary appointment<br>7 | |
| Moving Away<br>2 | Higher Salary | | Expiration of temporary appointment<br>8 | |
| Health | | | Abadmonment of position<br>3 | |
| Transportation | | | | |
| Personnel<br>5 | | | | |
| SUB-TOTALS<br>20 | 1 | 4 | 19 | 2 |

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FABRIC CARE
OPD
PHARMACY

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
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PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
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## FABRIC CARE DEPARTMENT

### I. MISSION AND GOALS

The primary objectives of the Fabric Care Department during Fiscal Year 1979 were to:

1. Provide quality fabric care services at the most reasonable cost consistent with the needs of patient care and research in the Clinical Center, and other N.I.H. installations on the Bethesda campus, the Poolsville animal farm, the Landau, Westwood, Auburn buildings, the Baltimore Cancer Research Center, and St. Elizabeth's Hospital

2. Renovate the dry cleaning plant in accordance with Environmental Health and Safety Standards

3. Install new flatwork ironer complete with primary and cross folders

4. Continue to review manpower requirements in an effort to keep the number of permanent, full-time positions to at least three positions below the authorized N.I.H. ceiling

5. Provide in-service training for all employees

6. Continue to improve the quality of service to the N.I.H. community at a reasonable cost

7. Complete the two to three year plan for replacing key personnel nearing retirment.

## II. ACTIVITIES

### A. Production

Laundry Operations:

| | |
|---|---|
| Pounds Washed and Finished | 1,827,791 |
| Pounds Dyed | 54,623 |

Dry Cleaning Operation:

| | |
|---|---|
| Pounds Dry Cleaned and Finished | 149,060 |

New Linen Stores:

| | |
|---|---|
| Items Issued | 38,433 |
| Items Repaired | 3,446 |
| Items Altered | 29,701 |
| New Items Fabricated | 234 |
| Opening Inventory | 155,494 |
| Purchases | 263,333 |
| Cost of Goods Sold | 225,168 |
| Stock Write-Off | 140 |
| Closing Inventory | 193,519 |

1. The Department was able to meet the normal Demands for service with no major problems and with three positions below the authorized ceiling.

2. New flatwork ironer complete with primary and cross folder was installed.

3. The Annual Environmental and Safety Survey was conducted by the Environmental Safety Branch, Biological Control Section, DRS.

4. Reduced budgeted overtime by 15%.

5. Reduced permanent full-time positions by four positions.

6. Reduced the 1979 budget by 4%.

7. Evaluated an electronic laundry supply dispensing system with excellent results.

8. The goal of 100% participation in the Combined Federal Campaign was achieved within three hours on the first day of the campaign.

9. The Chief of the Department served as the 1979 C.F.C. Co-ordinator for the Clinical Center.

B. Personnel

1. Three employees attended Basic Adult Education Classes - (888 man hours).
2. Four employees attended the Clinical Center's safety classes - (32 man hours).
3. Two employees attended Upward Mobility College - (362 man hours).
4. The Department provided training and work experience for three (3) Stay-In-School and two (2) Summer-Aid employees.
5. The Plant Superintendent attended the Eastern Institutional Laundry Manager's Training Institute in Philadelphia, PA., (40 man-hours) and the Clinical Center sponsored Supervisor's Training Course (40 man-hours).
6. The Chief of the Department attended the 39th Annual Educational Conference of the National Association of Institutional Laundry Managers in Chicago. He also attended the N.I.H. training course - Understanding and Managing Stress.
7. The Department provided a work therapy program for one Clinical Center patient.

## III. FUTURE OBJECTIVES

1. Renovate the dry cleaning plant in accordance with Environmental Health and Safety Standards.
2. Reduce budgeted overtime by 5%.
3. Reduce the 1980 budget by 7%.
4. Continue to review manpower requirements in an effort to reduce authorized permanent full-time ceiling by one position.
5. Replace the present outdated laundry supply dispensing system with a modern electronic dispensing system. This system will reduce the present cost of the laundry supplies by 47%.
6. Continue to participate in the Stay-In-School and the Summer-Aid programs.
7. Relocate the Receiving and Issue Room in the Clinical Center.

NUCLEAR MED.

MED. REC.

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OPD

PHARMACY

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
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MEDICAL RECORD DEPARTMENT

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October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

# MEDICAL RECORD DEPARTMENT

## DEPARTMENT MISSIONS AND GOALS

The Clinical Center Medical Record Department maintains a medical record and/or microfiche for every registered Clinical Center patient. The prime objective of the Medical Record Department is to insure that each medical record is complete, accurate, safeguarded, and available to authorized personnel. To this end systems are maintained which provide: 1) immediate access and release of medical records and/or microfiche and information to authorized users; 2) a computerized listing of each patient by diagnosis and operation; 3) an analysis by Institute of discharged inpatients; 4) a systematic arrangement of reports within the medical record; 5) transcribed medical reports and communication with referring physicians.

## ACTIVITIES AND PROGRESS

### Education and Training

One medical record administrator successfully passed the National Registration Examination for medical record administrators.

Orientation was held for employees from Clinical Center Departments and Institutes. Lecture tours were given to USPHS student medical record administrators, clinical associates, and students participating in the Clinical Electives Program.

A number of Medical Record Department employees were honored at the Annual Clinical Center Awards Ceremony in September.

Personnel attended a variety of workshops to enhance work knowledge for such subjects as record management, microfilming techniques, and coding of disease and operation applications.

### Activities and Progress

Major emphasis was placed on promoting medical record consciousness among physicians and ancillary services. To achieve this end, the Chief of the Medical Record Department was a member of several ad hoc committees actively studying the utility and growth of the computerized medical record.

Proposals from contract bidders were received and technical evaluations performed for off-site transcription service. In January 1979 four contractors were awarded a three-year negotiated contract for transcription of medical reports. In March 1979 one contractor was awarded a three-year negotiated contract for transcription of outpatient letters.

Problem solving sessions were held with the microfilm contractor to assure the 62,000 medical records targeted for conversion to microfiche meet production schedules. Progress for FY 1979: approximately 28,000 medical records have been prepared for the microfilming process; approximately 12,000 microfiche have been inspected and meet archival standards. The contractor has affirmed that FY 1979 production cycle will meet specified target dates.

To keep abreast of an average of 32 medicolegal requests per day an additional employee was hired for the Medicolegal Section. These requests included Privacy Act cases where patients utilized the medical record access privilege.

The classification conversion for the coding of inpatient diagnoses and operations was undertaken. The conversion utilized a change of texts entitled Eighth Revision International Classification of Diseases, Adapted (ICDA-8) to International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). However, computer program changes hampered full implementation, consequently dual coding has transpired since January 1979.

Seven medical audits were completed. The Medical Record Department played a key role in abstracting and tabulating the required data and participated in the ongoing analysis required by the Audit Committee.

# WORK PRODUCTION STATISTICS

July 1, 1978 to June 30, 1979 - Actual
July 1, 1979 to September 30, 1979 - Projected

| | Column A 7-1-78/6-30-79 (Actual) | *Column B 7-1-79/9-30-79 (Projected) | Column C TOTAL |
|---|---|---|---|
| I. Medicolegal Section | | | |
| Total number of requests | 7,494 | 945 | 8,439 |
| Average requests per day | 29 | 31 | 30 |
| II. Record Processing Section | | | |
| Incomplete records as of 6-30-79 | 1,398 | -- | -- |
| Incomplete records as of 9-30-79 | -- | 1,132 | 1,265 |
| III. Files Section - Record Circulation | | | |
| Complete Records | 19,270 | 4,771 | 24,041 |
| Clinics & Admissions | 51,688 | 14,775 | 66,463 |
| Incomplete Records | 7,550 | 66,463 | 9,344 |
| IV. Transcribing Section** | | | |
| Cassettes received | 14,111 | 3,517 | 17,628 |
| Cassettes transcribed | 14,204 | 3,621 | 17,825 |

** Figures for cassettes transcribed are greater than cassettes received due to cassettes remaining at beginning of the month.

* Projected figures 7-1-79/9-30-79 are based on actual figures 7-1-78/9-30-78.

## PROBLEMS

1. The number of delinquent medical records exceed JCAH's recommended number significantly despite the varied attempts to remedy the problem.

2. Source documents resulting from MIS input: 1) do not contain accurate information to allow the Medical Record Department to effectively attain completion of the medical record, 2) many documents are generated, which contain "no medical data" thus contributing to a voluminous medical record.

3. A critical shortage of filing space for active medical records has necessitated full utilization of the satellite storage area in B2L406.

## OBJECTIVES

1. Physical reorganization in the Record Processing Section. Utilize modules to allow more work area for the clerks while physically occupying less floor space. Consequently, more room will be provided for the physician who must review and/or dictate clinical reports and allow for an efficient workflow.

2. Implement the use of the automated equipment designed to track and find medical records.

3. Plan for off-site storage of 64,000 inactive and multipart current medical records now located in Building 10, Room B2L406.

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

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# MEDICAL RECORD DEPARTMENT

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October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## MEDICAL RECORD DEPARTMENT

## DEPARTMENT MISSIONS AND GOALS

The Clinical Center Medical Record Department maintains a medical record and/or microfiche for every registered Clinical Center patient. The prime objective of the Medical Record Department is to insure that each medical record is complete, accurate, safeguarded, and available to authorized personnel. To this end systems are maintained which provide: 1) immediate access and release of medical records and/or microfiche and information to authorized users; 2) a computerized listing of each patient by diagnosis and operation; 3) an analysis by Institute of discharged inpatients; 4) a systematic arrangement of reports within the medical record; 5) transcribed medical reports and communication with referring physicians.

## ACTIVITIES AND PROGRESS

### Education and Training

One medical record administrator successfully passed the National Registration Examination for medical record administrators.

Orientation was held for employees from Clinical Center Departments and Institutes. Lecture tours were given to USPHS student medical record administrators, clinical associates, and students participating in the Clinical Electives Program.

A number of Medical Record Department employees were honored at the Annual Clinical Center Awards Ceremony in September.

Personnel attended a variety of workshops to enhance work knowledge for such subjects as record management, microfilming techniques, and coding of disease and operation applications.

### Activities and Progress

Major emphasis was placed on promoting medical record consciousness among physicians and ancillary services. To achieve this end, the Chief of the Medical Record Department was a member of several ad hoc committees actively studying the utility and growth of the computerized medical record.

Proposals from contract bidders were received and technical evaluations performed for off-site transcription service. In January 1979 four contractors were awarded a three-year negotiated contract for transcription of medical reports. In March 1979 one contractor was awarded a three-year negotiated contract for transcription of outpatient letters.

Problem solving sessions were held with the microfilm contractor to assure the 62,000 medical records targeted for conversion to microfiche meet production schedules. Progress for FY 1979: approximately 28,000 medical records have been prepared for the microfilming process; approximately 12,000 microfiche have been inspected and meet archival standards. The contractor has affirmed that FY 1979 production cycle will meet specified target dates.

To keep abreast of an average of 32 medicolegal requests per day an additional employee was hired for the Medicolegal Section. These requests included Privacy Act cases where patients utilized the medical record access privilege.

The classification conversion for the coding of inpatient diagnoses and operations was undertaken. The conversion utilized a change of texts entitled Eighth Revision International Classification of Diseases, Adapted (ICDA-8) to International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). However, computer program changes hampered full implementation, consequently dual coding has transpired since January 1979.

Seven medical audits were completed. The Medical Record Department played a key role in abstracting and tabulating the required data and participated in the ongoing analysis required by the Audit Committee.

## WORK PRODUCTION STATISTICS

July 1, 1978 to June 30, 1979 - Actual
July 1, 1979 to September 30, 1979 - Projected

| | Column A<br>7-1-78/6-30-79<br>(Actual) | *Column B<br>7-1-79/9-30-79<br>(Projected) | Column C<br>TOTAL |
|---|---|---|---|
| I. Medicolegal Section | | | |
| Total number of requests | 7,494 | 945 | 8,439 |
| Average requests per day | 29 | 31 | 30 |
| II. Record Processing Section | | | |
| Incomplete records as of 6-30-79 | 1,398 | -- | -- |
| Incomplete records as of 9-30-79 | -- | 1,132 | 1,265 |
| III. Files Section - Record Circulation | | | |
| Complete Records | 19,270 | 4,771 | 24,041 |
| Clinics & Admissions | 51,688 | 14,775 | 66,463 |
| Incomplete Records | 7,550 | 66,463 | 9,344 |
| IV. Transcribing Section** | | | |
| Cassettes received | 14,111 | 3,517 | 17,628 |
| Cassettes transcribed | 14,204 | 3,621 | 17,825 |

** Figures for cassettes transcribed are greater than cassettes received due to cassettes remaining at beginning of the month.

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* Projected figures 7-1-79/9-30-79 are based on actual figures 7-1-78/9-30-78.

## PROBLEMS

1. The number of delinquent medical records exceed JCAH's recommended number significantly despite the varied attempts to remedy the problem.

2. Source documents resulting from MIS input: 1) do not contain accurate information to allow the Medical Record Department to effectively attain completion of the medical record, 2) many documents are generated, which contain "no medical data" thus contributing to a voluminous medical record.

3. A critical shortage of filing space for active medical records has necessitated full utilization of the satellite storage area in B2L406.

## OBJECTIVES

1. Physical reorganization in the Record Processing Section. Utilize modules to allow more work area for the clerks while physically occupying less floor space. Consequently, more room will be provided for the physician who must review and/or dictate clinical reports and allow for an efficient workflow.

2. Implement the use of the automated equipment designed to track and find medical records.

3. Plan for off-site storage of 64,000 inactive and multipart current medical records now located in Building 10, Room B2L406.

NUCLEAR MED.

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October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES

CLINICAL CENTER

DEPARTMENT OF NUCLEAR MEDICINE

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SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES

CLINICAL CENTER

DEPARTMENT OF NUCLEAR MEDICINE

## DEPARTMENT MISSIONS AND GOALS

### Applied Physics Section

The Applied Physics Section performs two basic functions: 1) to supply technical and professional assistance to the Department of Nuclear Medicine and other investigators in the resolution of selected diagnostic and experimental problems requiring Nuclear Medicine technology and 2) to independently develop novel diagnostic procedures, from concept through hardware, aimed at resolving selected problems of medical diagnosis.

### Diagnostic Imaging Section

This Section serves the clinical research goals of the NIH through the *in vivo* diagnostic use of radioactive pharmaceuticals to evaluate diseases that are under study in the Clinical Center in- and outpatients. This information helps physicians to choose and assess therapy. Major goals are to improve existing techniques and to develop new techniques that have minimal morbidity for the patient. Consultation is provided by the department's physicians who interview and administer radiopharmaceuticals to all referred patients.

### Radiopharmaceutical Section

The major responsibilities of the Radiopharmaceutical Section are its service functions, quality control efforts, and involvement in the dose dispensing system employed in the Diagnostic Imaging Section. Services consist of the procurement, receipt, registration, formulation, and development of all radiopharmaceuticals intended for use in Clinical Center patients. Quality control efforts consist of assaying, radiochemical and radionuclide purity checks, pH determination, particle sizing, and a host of other considerations necessary to establish the pharmaceutical quality of the products.

### Whole Body Counter Section

The NIH Whole Body Counter Section provides the NIH community with a unique facility for direct quantitative measurements of uptake and retention of biologically active materials and trace elements labeled with gamma-ray emitting radionuclides; it evaluates the amount and identifies unknown radionuclides in the human body. This Section also serves as a source of information and support for investigators who wish to design special counting systems for the measurement of biological supplies containing radionuclides.

## DEPARTMENT ACTIVITIES

### Applied Physics Section

In accord with its mission, the Applied Physics Section continued its collaborative efforts with National Heart, Lung, and Blood Institute/Cardiology Branch, Division of Computer Research and Technology/Laboratory of Applied Studies, and DCRT/Computer Systems Laboratory during FY 79 in the pursuit of noninvasive methods for detecting, diagnosing, and quantifying cardiac disease.

Imaging equipment, work space, and expendables were provided by Nuclear Medicine/Clinical Center and DCRT. Radiopharmaceuticals were provided by the Radiopharmacy Section/NM.

### Diagnostic Imaging Section

The imaging equipment necessary to achieve the above mission requires continued upgrading. The field of nuclear medicine is fast changing and demands a constant refreshment of departmental physician and technician knowledge. Electronic equipment is costly and is under continual development by private industry. Medical diagnostic capability can be improved and maintained only if a program of continued, well chosen acquisition of newly available electronic devices is followed.

The Department did not purchase any new major equipment in FY 79; however, NINCDS purchased a new device (positron scanner) which is to be placed in the Nuclear Medicine Department, who will supervise its use. A new radiochemistry laboratory has been constructed in Building 21 as an adjunct to this new piece of equipment. A radiochemist has also joined the Department of Nuclear Medicine to provide positron labeled compounds for use with this new device.

## Radiopharmaceutical Section

Approximately 87% of the total requests and workload of this Section is directly serviced by the Diagnostic Imaging Section. The future workload can be anticipated to be proportional to that of the Diagnostic Imaging Section in regard to its usage of radionuclide products.

A radiopharmacist continued to be involved in the dosing area for approximately 30 man hours per week. The radiopharmacist effectively controlled and dispensed radiopharmaceuticals and insured the practice of good radiation safety principles.

The 21% increase in expenditures was contributed to by inflationary trends plus approximately $10,000 for pyrophosphate kits for the *in vivo* labeling of red blood cells.

## Whole Body Counter Section

During FY 79, the Section experienced a near doubling of requested research and diagnostic studies. In large part this was due to increased $^{65}$Zn metabolism studies involving 3575 patient measurements in FY 79. The Whole Body Counter Section has emphasized medical research measurements for the past seven years, and will continue to do so during FY 80. Efforts to inform the NIH community of the availability of our services will continue to include the distribution of an informative pamphlet (Whole Body Counter Handbook, DHEW Pub. No. NIH 78-348) and presentation of information about whole body counting and other available services through Division of Research Services and Radiation Safety Branch teaching programs for licensed investigators who use radionuclides. Appended tables provide a complete breakdown of the numbers and types of studies performed by the Section in 1979. The Whole Body Counter staff was involved in publication of five papers (3 published, 2 in press), and presentation of two papers (one at the Annual Federation of American Societies for Experimental Biology in Dallas, Texas, and one to the American Clinical Research Society in Washington, D.C. It is anticipated that several more papers detailing results of Whole Body Counter Section Research will be published in FY 80.

## MAJOR PROGRESS IN RESEARCH, TRAINING AND DEVELOPMENT

### Applied Physics Section

Four objectives were attained by the APS during FY 79 in support of collaborative projects with other NIH organizations: (1) APS technical and scientific support continued, as planned, throughout FY 79 as part of a large scale clinical evaluation of gated blood pool imaging at rest and during exercise in patients with a variety of cardiac disorders (CB/NHLBI, APS); (2) the Section acquired and implemented the capability for "distributed" data processing, both to support the above clinical investigations while also providing for expanded overall computer systems usage (APS, CSL/DCRT); (3) continued development and evaluation of a portable probe device capable of direct, continuous monitoring of left ventricular function simultaneously with other physiologic parameters (CSL/DCRT, APS); (4) continued projects and initiated others designed to determine the absolute accuracy of gated blood pool imaging and to absolutely quantitate left ventricular volume.

### Diagnostic Imaging Section

Computerized axial tomography, as in FY 78, remains as a new frontier in Nuclear Medicine. It will take some years before the potential benefits are realized. A positron scanning device has been purchased by NINCDS and should be at NIH (CC/NM) by the beginning of FY80.

Gated cardiac blood pool and pulmonary studies continue in collaboration with NHLBI and DCRT.

A radiochemistry laboratory has been established in Bldg. 21 and two radiochemists will join the Department as part of the NIH positron research project.

### Radiopharmaceutical Section

Research efforts consisted of developing and labelling In-111 Macroaggregated Human Serum Albumin and In-111 Microspheres for potential use in lung perfusion studies. The Section also evaluated 3 different chromatogram scanners used for the determination of radiochemical purity of labelled compounds and was involved in drug incompatibility studies of radiopharmaceuticals in commonly used IV additives.

A total of 20 different radionuclides were received which constituted 69 different products formulation (see Table). Products not previously received or formulated were Technetium-99m Iprofenin, In-111 Macroaggregated Human Serum Albumin and In-111 Microspheres.

## Radiopharmaceutical Section (continued)

The radiopharmacy also provided a preceptorship for two students from the Duquesne University School of Pharmacy Controlled Externship Program and, in addition, trained two pharmacy students within the COSTEP. Lectures and consultative functions were also rendered to paramedical personnel regarding various aspects of radiopharmacy.

## Whole Body Counter Section

During FY 79 the Whole Body Counter Section acquired a plotting output writer to add plotting and typed copy capabilities to the Wang 2200B computer. There were no other major purchases made during FY 79. The Section also purchased electronic components for several counting systems. We anticipate the need to replace several counting systems in the near future.

The Whole Body Counter Section experienced a large increase in research measurements in FY 79, primarily due to a cooperative study of $^{65}$Zn metabolism with the Center for Molecular Nutrition and Sensory Disorders of the Georgetown University Medical Center. This increase is not expected to continue beyond FY 80.

Personnel monitoring measurements increased by 7% during FY 79 and are expected to continue growing at this rate or greater.

## FUTURE OBJECTIVES TOWARD MEETING GOALS:

## Applied Physics Section

Clinical studies with the real-time cardiac imaging system will continue. Refinements of this system through appropriate software and hardware changes will also be continued.

The portable probe system will be further exploited in intervention studies in the Catheterization Laboratory and elsewhere. Investigations of the accuracy, precision, and assumptions underlying the scintigraphic method will be continued.

## Diagnostic Imaging Section

Departmental Research: New radiopharmaceuticals are under development for pulmonary studies (inhalation lung scans). For the positron program a future objective under consideration by NIH is the acquisition of a cyclotron, a project which will take several years to realize, if it is decided that there is a need for a cyclotron at NIH. If the benefits of a positron program are to be realized, it appears that a cyclotron will be required.

Departmental Operation: Improved staffing and operation of the clerk-receptionist areas is a current objective. Other objectives are the gradual acquisition of new equipment for imaging procedures.

## Radiopharmaceutical Section

The future objectives of the Section are to continue to collaborate with the service and research efforts of the Diagnostic Imaging Section and other Clinical Center investigators with involvement in the formulation, development, and quality control of all radiopharmaceutical products intended for patient administration.

The projected utilization of positron emitting radionuclides will increase the radiopharmacy's duties in new aspects pertaining to the chemistry and pharmaceutical quality control assurances of the labelled products.

## Whole Body Counter Section

Future objectives of the Section include continuing a program of expanding services to encompass an increasing range of research services, refinement of the Section's current support capabilities in the areas of human metabolism and nutrition, and the continuing development of clinical support from investigators who are presently unaware of the potential of whole body counting in their research programs.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 00007-04 NM |

PERIOD COVERED
October 1, 1978 through September 30, 1979

TITLE OF PROJECT (80 characters or less)

ECG-Gated Scintigraphic Angiocardiography

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | J.S. Borer | Senior Investigator | CB NHLBI |
| | S.L. Bacharach | Physicist | NM CC |
| | M.V. Green | Chief, Applied Physics | NM CC |
| OTHER: | K.M. Kent | Senior Investigator | CB NHLBI |
| | J.J. Bailey | Head, MAS | LAS DCRT |
| | M.A. Douglas | Programmer | LAS DCRT |
| | H.G. Ostrow | Engineer | CSL DCRT |

COOPERATING UNITS (if any)
CB NHLBI
LAS DCRT
CSL DCRT

LAB/BRANCH
Department of Nuclear Medicine, CC

SECTION
Applied Physics Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

High temporal resolution ECG-gated scintigraphic angiocardiography (radionuclide cineangiography) is a computer-based, radiotracer imaging procedure that allows non-invasive visualization of the chambers of the working heart at rest, during bicycle exercise, during therapeutic intervention, etc. The procedure yields quantitative measures of left ventricular function such as ejection fraction, peak ejection rate, etc. Work is continuing to assess the accuracy of these data in man and to establish findings for the method in selected disease categories. Variations of this technique are being explored and will result in an inexpensive, portable device capable of continuous real-time measurement of left ventricular function.

## Project Description

### Objectives:

To continue to validate, develop and exploit ECG-gated scintigraphy (radionuclide cineangiography) and its variants in the detection, evaluation and quantitation of cardiac disease in man.

### Methods Employed:

Comparative clinical studies were continued during FY 79 (CB/NHLBI, APS) under the rest-exercise imaging protocol. Studies were continued to: (1) compare, in large patient populations, the sensitivity and specificity of radionuclide cineangiography with other established diagnostic procedures in the detection of coronary artery disease; (2) to ascertain the effects of surgical therapy on the exercise response of the left ventricle; (3) to ascertain the exercise response of the left ventricle following myocardial infarction; (4) to ascertain the effects of balloon dilation of the coronary arteries on ventricular performance; (5) to assess the exercise response of the ventricle to various medications and (6) to ascertain the effect of exercise on ventricular performance in the presence of other cardiac abnormalities.

Technical support of these efforts was continuous throughout FY 79 with some 800 patients being studied (APS). Scientific support for this project resulted in the implementation of a distributed data processing system capable of keeping pace with the scope of the effort above while at the some time providing expanded computer capability for other system users (APS). Scientific support continued toward development of reliable, fully automated data reduction algorithms for use in these cardiac studies. Several algorithms resulting from these investigations have been implemented in the real-time imaging system and are now being clinically tested (LAS/APS).

Basic investigations into the accuracy, precision and assumptions underlying these radionuclide studies were also continued during FY 79. Using an extremely high sensitivity scintillation probe, (CSL/APS) the time variation of left ventricular volume appears to be measurable with good precision during individual cardiac cycles (not heretofore possible). These data can be directly used to verify the effects of gating these same data. Completion of this work should permit definite quantitative conclusions to be drawn regarding the validity of several major assumptions required by radionuclide cineangiography.

Preliminary investigations were also initiated to evaluate several possible methods by which absolute ventricular volumes might be determined, a capability lacking at present.

Development and evaluation of a portable probe system were continued during FY 79. The present system has been used successfully in the catheterization laboratory to construct left ventricular pressure - volume loops in real time. This and other applications will be pursued in the forthcoming year.

### Findings:

Representative scientific and clerical findings are detailed in the references.

### Significance of the Research Program:

Radionuclide cineangiography is demonstrably useful in the detection and in the management of patients with cardiac disease. This procedure requires only an intravenous injection of radiotracer and is otherwise utterly non-invasive. It is rapid, safe and can be repeated under varying circumstances such as exercise, medication, etc., for a period of hours, without further tracer administration. This characteristic also makes the technique suitable for continuous LV function monitoring. This application is being exploited through development of a portable probe system which will be employed in special measurement situations.

### Proposed Course:

Continuation of the work.

### Honors and Awards:

None.

### Publications:

1. Bacharach, S.L., Green, M.V., Borer, J.S., Hyde, J.E., Farkas, S.P., Johnston, G.S.: Left ventricular peak ejection rate, filling rate and ejection fraction: Frame rate requirments at rest and exercise. Journal of Nuclear Medicine 20:189-193, 1979.

2. Green, M.V., Ostrow, H.G., Douglas, M.A., Scott, R.N., Bailey, J.J., Johnston, G.S.: A comparison of simultaneous measurements of systolic function in the baboon by electromagnetic flowmeter and high frame rate ECG-gated blood pool scintigraphy. Circulation (in press) August 1979.

3. Borer, J.S., Bacharach, S.L., Green, M.V.: Evaluation of the patient with valvular heart disease: use of radionuclide cineangiography during exercise. Cardiology Update, E. Rapaport ed. Elsevier, N.Y. 1979.

## TABLE I

Comparison of Whole Body Measurements
for Fiscal Years 1978 and 1979

| | Isotope | 1978 | 1979* |
|---|---|---|---|
| Research Studies | | | |
| | Ca-47 | 24 | 15 |
| | Ga-67 | 21 | 0 |
| | Zn-65 | 1 | 3075 |
| | Cr-51 | 134 | 0 |
| | K -40 | 70 | 140 |
| | I -131 | 1349 | 1065 |
| | I-123 | 71 | 5 |
| | | 1670 | 4300 |
| Personnel Monitoring Studies | | | |
| | I-125, 131 | 1820 | 1860 |
| | Whole Body | 740 | 880 |
| | | 2560 | 2740 |

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*Fiscal Year 1979 values estimated from 10/78 through 6/79 plus scheduled increases, expressed as yearly rates.

## TABLE II

### Other Analysis Related to Whole Body Metabolism Studies

| | FY 1978 | FY 1979 |
|---|---|---|
| **Excreta Studies** | | |
| Zn-65 | 0 | 1680 |
| Cr-51 | 40 | 12 |
| | 40 | 1692 |
| | 126 | 40 |
| **Blood Studies** | | |
| Samples Taken | 28 | 1177 |
| Red Cell Washings | 28 | 1165 |
| | 56 | 2342 |
| **Blood Counts** | | |
| Ca-47 | 27 | 12 |
| Zn-65 | 1 | 2330 |
| | 28 | 2342 |
| **Tissue Sample Counting** | | |
| Sr-85, Ce-144 Yb-169, Sc-46 | 2835 | 1410 |
| **Dose Calibrations** | | |
| I-131 | 883 | 710 |

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*Fiscal Year 1979 values estimated from 10/78 through 6/79 plus scheduled inceases expressed as yearly rates.

## TABLE III

### Twelve Year Record of Whole Body Measurments

| Year | Research Measurements | % of Total | Personnel Measurements | % of Total | Total Measurments | Yearly % Change | Yearly % Change from 1968 |
|---|---|---|---|---|---|---|---|
| 1968 | 1102 | 67 | 552 | 33 | 1654 | --- | --- |
| 1969 | 639 | 60 | 427 | 40 | 1066 | -36 | -36 |
| 1970 | 234 | 31 | 511 | 69 | 745 | -30 | -55 |
| 1971 | 317 | 36 | 566 | 64 | 883 | 19 | -47 |
| 1972 | 1168 | 71 | 476 | 29 | 1644 | 86 | -0.6 |
| 1973 | 1863 | 64 | 1030 | 36 | 2893 | 76 | 75 |
| 1974 | 2138 | 68 | 1292 | 38 | 3430 | 19 | 107 |
| 1975 | 3615 | 68 | 1721 | 32 | 5336 | 56 | 223 |
| 1976 | 2311 | 52 | 2135 | 48 | 4446 | -18 | 163 |
| 1977 | 1485 | 44 | 1921 | 56 | 3406 | -23 | 106 |
| 1978 | 1670 | 39 | 2560 | 61 | 4230 | 24 | 156 |
| 1979 | 4800 | 64 | 2740 | 36 | 7540 | 78 | 356 |

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*Fiscal Year 1979 values derived from 10/78 through 6/79 work load plus an estimation for 7/79 through 9/79.

## Table IV

## Radiopharmaceutical Section Statistical Data

| | FY-78 | *FY-79 | % Change |
|---|---|---|---|
| Service Requests | 2,208 | 1,995 | - 10% |
| Work Units | 25,200 | 23,492 | - 7% |
| Unit Dose Requests | 6,506 | 6,663 | + 2% |
| RPS Assays | 4,090 | 3,876 | - 5% |
| Radionuclidic Purity Checks | 513 | 552 | + 8% |
| RPS Expenditures | $104,157.68 | $126,309.20 | + 21% |

* = FY-79 - projected figure

Table V

Radionuclides and Products Received, Registered, and Formulated - FY 79

| | | | |
|---|---|---|---|
| 1. | H-3 | - | Dehydro[7(N)-H-3]epiandrosterone Sulfate (K+ Salt)<br>Estradiol [6,7-H-3(N)]<br>Estrone [2,4,6,7-H-3(N)]<br>Estrone [6,7-H-3(N)] |
| 2. | C-14 | - | Alanine<br>Dopamine<br>Glucose, D [C-14(U)] |
| 3. | P-32 | - | Chromic Phosphate Suspension |
| 4. | Ca-47 | - | Calcium Chloride |
| 5. | Cr-51 | - | Erythrocytes<br>Human Serum Albumin<br>Sodium Chromate |
| 6. | Co-57 | - | Cyanocobalamin Capsules |
| 7. | Co-58 | - | Cyanocobalamin Capsules |
| 8. | Fe-59 | - | Ferrous Citrate<br>Plasma |
| 9. | Ga-67 | - | Gallium Citrate |
| 10. | Se-75 | - | Selenomethionine |
| 11. | Kr-85 | - | Krypton Gas |
| 12. | Mo-99 | - | Mo-99/Tc-99m Generator |
| 13. | Tc-99m | - | Diethylenetriaminepentaacetic Acid<br>Diphosphonate<br>Iprofenin<br>Macroaggregated Human Serum Albumin<br>Methylene Diphosphonate<br>Sodium Pertechnetate<br>Stannous Human Serum Albumin<br>Sulfur Colloid |
| 14. | In-111 | - | Diethylenetriaminepentaacetic Acid<br>Indium Chloride<br>Macroaggregated Human Serum Albumin<br>Microspheres |

15. I-123 - Sodium Iodide Oral Solution
    Sodium-o-Iodohippurate

16. I-125 - A-1 High Density Lipoprotein
    A-2 High Density Lipoprotein
    A-1 Lipoprotein
    A-2 Lipoprotein
    Alpha-1-Antitrypsin-Z
    Apo-E High Density Lipoprotein
    Apolipoprotein C-II
    Fibrinogen
    Hemopexin
    High Density Lipoprotein
    Human Serum Albumin
    Insulin
    Lipthyronine
    Reverse T-3
    Thyroxine
    Very Low Density Lipoprotein

17. Xe-127 - Xenon Gas

18. I-131 - A-1 High Density Lipoprotein
    A-2 High Density Lipoprotein
    A-1 Lipoprotein
    A-2 Lipoprotein
    Alpha-1-Antitrypsin-M
    Apolipoprotein C-III
    Human Serum Albumin
    Lipthyronine
    Low Density Lipoprotein
    Pro-Insulin
    Sodium Iodide Oral Solution
    Sodium Iodide Uptake Solution
    Sodium-o-Iodohippurate
    T-3

19. Xe-133 - Xenon Gas
    Xenon in Saline
    Ventilation Study System

20. Tl-201 - Thallous Chloride

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## TABLE VI
## Diagnostic Nuclear Medicine Section

### Patient Visits by Fiscal Year

| Date | 1967 | 1968 | 1969 |
|---|---|---|---|
| Total | 2568 | 3093 | 1637 |
| Yearly % Change | | 20% | 47%* |
| Yearly % Change from 1967 | | 20% | 36%* |

| Date | 1970 | 1971 | 1972 |
|---|---|---|---|
| Total | 2181 | 2308 | 2950 |
| Yearly % Change | 33%* | 0% | 28% |
| Yearly % Change from 1967 | 15%* | 7%* | 15% |

| Date | 1973 | 1974 | 1975 |
|---|---|---|---|
| Total | 4688 | 7039 | 7098 |
| Yearly % Change | 59% | 50% | 0% |
| Yearly % change from 1967 | 82% | 174% | 176% |

| Date | 1976 | 1977 | 1978 |
|---|---|---|---|
| Total | 8054 | 10056 | 9074 |
| Yearly % Change | 13% | 25% | 10%* |
| Yearly % Change from 1967 | 214% | 282% | 253% |

| Date | 1979 |
|---|---|
| Total | 8200 |
| Yearly % Change | 10%* |
| Yearly % Change from 1967 | 219% |

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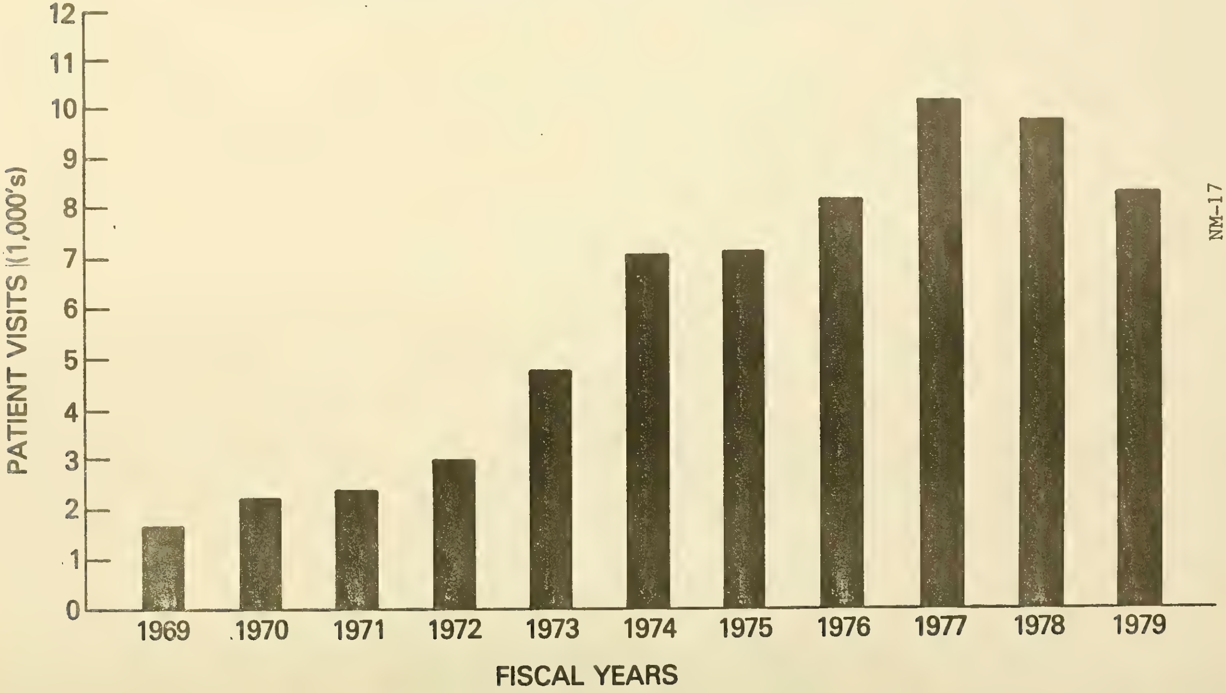
* Decrease

1978/79 X-Ray Computerized Tomography Studies Transferred to X-Ray Department/CC

GROWTH OF CLINICAL CENTER NUCLEAR MEDICINE SERVICE TO NIH PATIENTS



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# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
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## NURSING DEPARTMENT

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# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## NURSING DEPARTMENT

### I. Department Missions and Goals

The Nursing Department at the Clinical Center exists to provide nursing services to patients and support to their families in a biomedical research environment. In addition to clearly identifiable and time-honored nursing practices, the Nursing Department assumes the responsibility for many expanding nursing activities recognized as physician services by the Joint Physician-Nurse Committee of the NIH Medical Board.

With the involvement of the entire Nursing Department and leadership provided by Nursing Department's Administrative Council, we revised our philosophy and defined goals. (Attachments I and II). We now emphasize a humanistic nursing theory to support biomedical research. To accomplish this mission the following goals were established for the Nursing Department:

1. To have accountable, ethical, documented nursing PRACTICE.
2. To have nursing SERVICES SUPPORT which facilitates nursing practice.
3. To have nursing EDUCATIONAL PROGRAMS which augment nursing practice.
4. To have a nursing RESEARCH PROGRAM which improves patient care.
5. To occupy a local, national, and international position of pre-eminence in nursing.

Objectives to achieve the mission of the Department, as expressed in the philosophy and goals, are developed annually by each nursing unit. In addition, each nurse in a major leadership role is required to develop individual goals assuring accountability for a major program area.

Goal achievement is monitored and recorded in the quarterly reports to Clinical Center management and through twice yearly briefing sessions with the Chief and Deputy Chief of the Nursing Department. Significant accomplishments, problems, and recommendations are addressed.

### II. Department Activities

A. The recruitment and retention of staff in numbers and competence to support the research activities of the Institutes remain a major activity. With a limited personnel ceiling to achieve the research and patient care mission and with accreditation and nurse practice acts compliance expected, professional nurses with experience and more recent educational attainments are better able to provide the required services 24 hours a day, 7 days a week. In addition, with broader implementation of the primary nursing system which is both attractive and provides greater satisfaction to patients and staff, a majority of the staff must be professional nurses. The turnover rate for FY '78 was 20%, while for FY '77 it was 21% Department-wide. The excessively high turnover rate of 74% on the Open Heart Surgery Unit is a major concern. Employment freezes have a deleterious effect and hamper an uninterrupted recruitment effort in a highly competitive market locally and nationally. (Attachment III).

B. An administrative request to reduce the use of overtime was followed. The Nursing Department began to monitor this activity vigorously. Overtime was reduced by more than 1000 hours per quarter.

C. In order to spread the workload more equitably among the nurses assigned to the Cancer Nursing Service, pediatric chemotherapy nurses who are assigned to the Outpatient Clinic are now providing weekend coverage for the Clinic.

D. Impressive committee and advisory group activities within the Nursing Department, with PHS Nursing and between nursing and clinical service Departments occurred. Two new liaison committees, each addressing patient care concerns, improved communications among care givers, continuity of care, and better discharge planning. They were:

Nursing Department and Social Work Department
Nursing Department and Rehabilitation Department

Members of the Nursing Department developed renewed interest and offered viable ideas for program direction. Frustration levels remain high among some nurses who, due to heavy workloads and frequent tour of duty rotations, have not been able to contribute to this dynamic process.

E. The retreat mechanism continues to provide various organized groups within the Nursing Department an opportunity to evaluate performance of the collective, raise concerns, problem solve, and plan for the future. Two groups chose outside facilitators; accomplishments have been significant in each group:

Administrative Council
Head Nurses
Clinical Nurse Experts
Clinical Nurse Educators
Staff Nurse Advisory Group

F. "Talk to the Chief," informal 30 minute conferences on all tours of duty have been initiated. In response to a major concern of care givers, two Departmental Time Planning Conferences with broad participation of nursing staff for creative planning were scheduled.

G. Administrative reorganization of the operating room was accomplished with the employment of a non-nurse manager and the abolishment of the position, Chief, Surgical Nursing Service. The Nursing Department continues to work with CC management in removing non-nursing activities from nursing, including appropriate management activities for which nursing knowledge and skills are not required.

H. On the retirement of the Chief, Eye Nursing Service and Arthritis and Metabolic Diseases Nursing Service, three nursing services were combined, Eye, Arthritis and Metabolic Diseases, and Child Health and Human Development with the assignment of one chief to administer the three services comprising five inpatient units and the outpatient programs.

I. Summer legislative interns from the ANA continue to begin and conclude their summer's experience with the Nursing Department. Five young women representing minority nurses in doctoral study funded by NIMH were articulate and goal directed. Following an absence of one summer, NLN nursing fellows, funded by the Robert Wood Johnson Foundation, spent an afternoon with the Administrative Council. Both groups were briefed on the activities of the Nursing Department, the mission of the CC and areas of mutual concern to nurses, with special emphasis on their legislative or executive branch office activities. The sharing of activities and impressions remain a highlight of our summer program.

J. The first Nursing Department Awards will be presented at the Sixth Annual Program Meeting of the Nursing Department scheduled for October. Committee activity for more than one year culminated with the development of criteria for the three awards:

Nurse of the Year
Distinguished Nurse
Recognition for Research Endeavors (Individual or Group)

A panel comprised of three nationally known nurses will select the recipients.

K. The Fifth Annual Research Meeting of the Nursing Department featured Jean Johnson, R.N., Ph.D. who addressed her research in a paper entitled, "Stress through Patient Preparation." The reaction panel, comprised of CC nursing staff members, provided recognition and has become a real source of pride for nursing.

## III. Major Progress in Research, Services, Training and Development

A. Significant progress has been possible this year as a result of the appointment of a doctorally prepared nurse who serves as Assistant for Research to the Chief, Nursing Department. In this role she serves as a resource to the Nursing Department's

Research and Review Committee which is in its fourth year. Consultations for research were provided to:

130 nurses, CC staff
41 students in Doctor of Nursing Science program - The Catholic University of America, School of Nursing
1 student in the master's program - University of Maryland, School of Nursing

1. Six research studies have been completed; nineteen are ongoing. (Attachment IV).

2. The first all-day workshop for nurses, "Nursing Research Proposal Review," was attended by thirty-three CC nurses. Future plans call for regularly scheduled sessions. Initially, consideration will be given to participation of nurses in academic settings and the surrounding community.

B. Services to patients.

1. Stress of care givers is a major concern. Multiple approaches are being utilized with much sharing of them at the service chief level.

   The Fall Annual Meeting featured a guest presentation, panel, and audience participation in "Burnout." Five well-known national nurse leaders joined us for the evening meeting, on the following day, and during the spring as the Nursing Department focused on staff concerns at the nursing unit and service level.

2. A five bed Critical Care Unit, with an expectation of nine beds, was activated in April under the newly created Clinical Center Critical Care Medicine Department. Nineteen nurses were initially assigned following a four week special orientation program. Twenty nurses are presently providing patient care services.

3. A four bed intermediate care unit has been created on the Open Heart Surgery Unit.

4. Renovation of the Endoscopy Suite was completed at the beginning of the fiscal year.

5. A Patient Care Concerns Subcommittee of the Nursing Practice Committee was formed on a staff member's suggestion and the need expressed by the Administrative Council.

6. Two members of the Nursing Department serve on the CC TV Advisory Board. Program plans for patient information on closed circuit TV are a major initiative.

7. Nursing provided leadership for the development of Patient Information handouts to patients for more than thirty-nine commonly

performed procedures. Notable examples are: Radiation Therapy, Endoscopy, Brain Scan, and EKG.

8. Proposal #11 presented to the Joint Physician-Nurse Committee was approved. This permits a selected, previously trained clinical nurse expert, Mental Health Nursing Service, to administer sympathomimetic and parasympathomimetic inhibitors by intravenous "push" infusion under medical supervision. Earlier initiatives recommended by the Joint Physician-Nurse Committee and subsequently approved have enhanced more active participation and understanding of nurses in bio-medical research endeavors.

9. The Nursing Department remains well represented in extramural committee and professional society activities through participation on the local, state, national, and international level. Papers have been presented, some publications finalized, and others are in press.

   a) Publications include:

      Barlock, A., Allegra, J. C., "Association Between Steriod Hormone Receptors and Responsive Rate to Cytoxic Chemotherapy in Metastatic Breast Cancer." Cancer Treatment Reports, Vol. 62, No. 9, Sept. 1978.

      Barlock, A., Hubbard, S., Howser, D., "Nursing Management of Adriamycin Extravasation." American Journal of Nursing, January 1979, pp. 94-96.

      Burks, J. and Griffith, P., "Iron Overload," Journal of Nursing Care, Sept. 1978, pp. 12-14.

      Crocker, E., Serotkin, M., Ferguson, V., Finkel, K., "Hospital Politics and Change: The Art of the Sometime Possible," Human Needs and Political Realities, 13th Annual Conference Proceedings of the Association for the Care of Children in Hospitals, June 5-8, 1978, Washington, D.C., pp. 15-28.

      Ferguson, V., "Closing Address," Proceedings of the Nursing Mirror International Cancer Nursing Conference, England, 1978, pp. 169-171.

      Hubbard, S., "Breast Cancer," Nursing Mirror, Dec. 7, 1978, pp. 31-36.

      Hubbard, S. M., "The Role and Function of the Chemotherapy Research Nurse," Proceedings of the Nursing Mirror International Cancer Nursing Conference, England, 1978, pp. 80-84.

      Lowery, S. F., Goodgamore, J. T., Smith, J. C., Maher, M. M., et al., "Abnormalities of Zinc and Copper During Total Parenteral Nutrition," Annals of Surgery, 189, January 1979, pp. 120-128.

Lowery, S. F., Goodgamore, Jr., J. T., Maher, M. M., Brennan, M. F., "Parenteral Vitamin Requirements During Intravenous Feeding," The American Journal of Clinical Nutrition, 31, December 1978, pp. 2149-2159.

Maher, M. M., Bowers, W. G., Thomas, G. M., Brennan, M. F., "An Improved Needle Adaptor for Central Venous Catheters," Journal of Parenteral and Enteral Nutrition, Vol. 3, No. 2, 1979, pp. 77-78.

McCalla, J. L., "Immunotherapy: Concepts and Nursing Implications," Cancer: Pathophysiology, Etiology and Management. Editors Krase, L. C., Reese, J. L., and Kart, L. K., St. Louis, The C. V. Mosby Company, 1979, pp. 239-247.

Taylor, M. L., "Mobilizing Nursing Department Resources to Improve Educational Programming," Journal of Nursing Administration, Dec. 1978, VIII:12, pp. 39-42

The following monographs of Clinical Conferences have been published:

Primary Nursing Care of the Pediatric Oncology Patient - Cancer Nursing Service
The Consultative Process in Mental Health Nursing - Mental Health Nursing Service

b) Significant Committee activity included:

1) Ms. Vernice Ferguson, Chief, Nursing Department, participated in the recently completed two year "Study of Credentialing in Nursing" funded by the ANA with sixteen members of multidisciplinary professionals represented and continuous input from forty-six cooperating groups and a study staff. The Deputy Surgeon General, PHS, and his staff were briefed on the study findings by the Chief Nurse.

The Chief Nurse continues to serve as the first Program Chairman for The American Academy of Nursing, ANA.

2) Ms. Susan Hubbard, Clinical Nurse Expert, Cancer Nursing Service, was elected to the Board of Directors, Oncology Nursing Society at the Fourth Annual Meeting.

c) Significant speaking engagements included:

1) Ms. Vernice Ferguson, Chief, Nursing Department and Ms. Jill Nusbaum, Head Nurse, Mental Health Nursing Ser-

vice -- Chautauqua '79: Diamond Jubilee.

2) Ms. Ruth Carlsen, Chief, Nursing Education, Mr. Max Gearhart, Chief, Mental Health Nursing Service, Ms. June McCalla and Ms. Regina Moses, Clinical Nurse Experts, Cancer Nursing Service -- Pennsylvania East - A Summer Symposium.

3) Ms. Audrey Barlock and Ms. Diane Howser, Clinical Nurse Experts, Cancer Nursing Service -- 12th International Cancer Conference - Buenos Aires, Argentina.

4) Ms. Vernice Ferguson, Chief, Nursing Department -- First Annual Conference for Nursing Service Research - University of Minnesota. First nurse lecturer - In-Center Lecture Series, Comprehensive Cancer Center for the State of Florida.

d) Significant Awards:

1) Ms. Vernice Ferguson, Chief, Nursing Department, received the Achievement Award for Nursing Services from the Nursing Education Alumni Association of Teachers College, Columbia University, New York, presented in recognition of distinguished achievement of alumni of the Department of Nursing Education.

2) Ms. Mary Curry, Clinical Nurse, Cancer Nursing Service, received the American Journal of Nursing/Maryland Nurses' Association 1978 Writing Award.

C. Training and Development

1. Since the initiation of the Central Nursing Office internship program in 1977, thirteen nurses, the majority of whom are staff nurses, have spent a week observing and participating in the chief nurse's activities. Six nurses will participate in FY 1980. This model has been extended to include all newly appointed nursing service chiefs, head nurses, clinical nurse experts, and clinical nurse educators. Recently, this preceptorship model has been extended to the nursing service level; most units have established a program to orient and support the new nurse which is in addition to the initial two week orientation program. The New Graduate Program was begun also. Feedback from participants in each of the programs is generally laudatory. The university model is also in place whereby graduate students utilize the resources of the Nursing Department while pursuing their practicum at the Clinical Center. They include:

The Catholic University of America - three master's level students in Community Health Nursing.

University of Maryland - two master's level students in Nursing Service Administration.

The Chief Nurse in her faculty associate role continues to conduct a seminar for all graduate students in this program. Negotiations are now in progress for the addition of two clinical nurse experts (pediatrics) to become faculty associates.

2. For the first time this year, students enrolled in the Doctor of Nursing Science program through the Nursing Department's contract with Catholic University have enhanced their research ability in study design and implementation of a project. The Nursing Department and several Institutes have extended opportunities to eleven students. Three have successfully completed their research studies.

3. In its third year, the Foreign Exchange Nurse Visitor Program, in collaboration with the National Cancer Institute, provided a six month exchange experience for the Chemotherapy Sister-in-Charge at the Royal Marsden Hospital in Surrey, England. One clinical nurse expert from the Cancer Nursing Service made a four month site visit to selected foreign cancer research centers and initiated a collaborative research project with medicine at one of these centers. Through the efforts of a newly created Screening Committee composed of Clinical Center nursing administrators and clinical nurse experts, the first American pediatric oncology nurse specialist from The North Carolina Memorial Hospital, University of North Carolina at Chapel Hill was assigned to the Christie Hospital in Manchester, England, for five months. Three American nurses were screened by the CC Nursing Department Committee.

4. The CC Nursing Department provided significant leadership to PHS Nursing in the approval of the ANA Continuing Education Program for PHS nurses nationwide. The Clinical Center Nursing Department was selected as the site for the accreditation visit of the ANA to a PHS facility. Sixteen Nursing Department courses were approved for USPHS continuing education in nursing credit (CEU). The USPHS program has been accredited by the ANA as a CEU provider for four years.

5. During its second year within FAES, the Nursing Department offered 15 courses with total attendance of more than 150 students; more than half are Clinical Center staff members. Eighteen courses will be offered during the fall semester, 1979.

6. Significant educational initiatives took place to assist nurses in providing care and assuming more active roles in implementing new research protocols. A new Intensive Care Nursing Course, a self-paced Nephrology Course I and II, and a Medical Information System (MIS) Concepts I Course were offered for CC-wide nurse participation. Nursing unit and service centered teaching rounds

were conducted by Neurosurgery and Eye Institute physicians. With the substantial development of the cytopheresis protocol, nurse reassignments have occurred on the Arthritis and Metabolic Diseases Nursing Service and with it, nurses on the service have developed new knowledge and skills, including A-V shunt and fistula care.

7. Sixteen members of the Administrative Council participated in a 20 hour course, "Bioethical Issues in Patient Care and Research," conducted by John Fletcher, Ph.D., Assistant for Bioethics to the Director, CC. The Deputy Chief Nurse was one of 60 people selected to participate in an intensive one week bioethics course for leaders in American medicine, nursing and health administration. This course was offered by the Joseph P. Kennedy, Jr. Foundation in collaboration with the Kennedy Institute of Ethics at Georgetown University. The Chief, Heart and Lung Nursing Service, participated in a week's course, sponsored by the Hastings Center, "The Teaching of Ethics," at Princeton, N.J. Of the 125 participants, ten were nurses.

8. An Infections Control course was added to our mandatory review sessions required of all nursing personnel. Four are now required; the others are:

   Cardiopulmonary Resuscitation
   Fire Safety Program
   Radiation Safety

9. Five nursing services held clinical conferences this year.

   a) Rheumatoid Arthritis - Arthritis and Metabolic Diseases Nursing Service

   b) Cancer Nursing Update '79 - Cancer Nursing Service

   c) Suicide Prevention: The Challenge for Nurses - Mental Health Nursing Service

   d) Primary Nursing in an Ambulatory Setting - Outpatient Nursing Service

   e) Nursing Care of the Patients with Thalassemia and Iron Overload - Heart and Lung Nursing Service

10. A clinical nurse, Cancer Nursing Service, received the American Nurses' Association certification for Medical-Surgical Nursing Practice.

11. The new position of Chief, Nursing Education was filled January 14, 1979 and marked the first step in the Nursing Department reorganization. As of June 30, 1979, five professionals and two non-professionals were assigned to Nursing

Education. Four clinical nurse educator positions will be reassigned through reorganization.

12. Ten head nurses and one service chief have been oriented to their respective assignments. All of the nurses continue to express disbelief at the complexity and dynamic state of the administrative process. Each nurse has cited particularly the ease of relating to the CC Director and his staff.

13. A nurse leader is being considered for the position vacancy, Chief, Mental Health Nursing Service.

## IV. Future Objectives Directed Toward Meeting Goals

The retreat mechanism and the Administrative Council forum mode will continue to be used to raise consciousness levels, identify issues and concerns, and solve problems. Developing creative solutions with the active participation of the nursing staff is encouraged. Committee and advisory group collective activity will continue to be encouraged. Our objectives will be focused during this year primarily on enhancing our professional practice and new program development through:

1. Inpatient-Outpatient program evaluation and Ambulatory Care Research Facility (ACRF) planning

2. Patient education initiatives

3. Critical care management, practice, and research

4. Developing a stronger nursing service identity and commitment rather than a sole unit identity

5. Greater use of nurse to nurse consultation

6. Maximal utilization of nurses for nursing with greater movement toward colleagueship and support to biomedical activities rather than non-nursing management

7. Improved communications.

# Clinical Center Nursing Department
# Philosophy

The Nursing Department of the Clinical Center is committed to supporting biomedical research through the provision of nursing care for patients and the support of their families and/or significant others. Our major goal is to provide individualized nursing service, utilizing Primary Nursing, which is consonant with the wide range of health-care requirements of patients in this setting.

Professional nursing at the Clinical center is defined as encompassing practice, administration, education, and research. Nursing is a clinical practice discipline. The nurse is responsible and accountable for utilizing the nursing process to assist the patient to achieve optimum health goals, or when a return to health is not possible to set new goals and initiate appropriate nursing action. Patients and those most closely involved with them should be active participants in the formulation and attainment of realistic health goals.

In nursing practice, we function both independently and interdependently. When meeting patient-care needs requiring nursing judgment, we function independently; when these needs require the involvement of others, we function collaboratively.

The goal of nursing administration, education and research is directed toward the continual improvement of nursing practice. We foster an environment in which staff members can acquire knowledge, increase clinical skills, demonstrate leadership, and participate in nursing research in order to establish a position of pre-eminence for professional nursing practice. We provide an environment which facilitates students' learning experiences.

Members of the Nursing Department adhere to a code of ethics. We are accountable for our actions to recipients of services for providing safe and competent care, to peers and the professional nursing community for setting and maintaining acceptable standards of care, to the institution for working in accord with organizational goals, and to the community-at-large for improving and contributing to the health care delivery system.

For Nursing Department Manuals

Formulation Date--------------------April, 1979----------

Implementation Date--------------------June, 1979----------

Review/Revision Date--------------------------------------

ATTACHMENT I

# CLINICAL CENTER

## NURSING DEPARTMENT GOALS

The mission of the Nursing Department is to support biomedical research through the provision of humanistic and theory based nursing care, care for patients, and support to their families or significant others. To accomplish this mission the goals follow:

1. To have accountable, ethical, documented nursing PRACTICE.
2. To have nursing SERVICES SUPPORT which facilitates nursing practice.
3. To have nursing EDUCATIONAL PROGRAMS which augment nursing practice.
4. To have a nursing RESEARCH PROGRAM which improves patient care.
5. To occupy a local, national, and international position of preeminence in nursing.

FORMULATED: 4/79
IMPLEMENTED: 6/79
REVIEWED:

ATTACHMENT II

## STAFFING DATA - NURSING DEPARTMENT

| | July 1, 1978 | June 30, 1979 |
|---|---|---|
| Total number of positions | 598 | 593 |
| Total number of positions filled | 605 | 607 |
| Total number of vacancies | +7 | +14 |
| **Administrative** | | |
| Total number of positions | 61 | 59 |
| Total number of positions filled | 54 | 54 |
| Total number of vacancies | -7 | -5 |
| **Clinical Instructors** | | |
| Total number of positions | 10 | 8 |
| Total number of positions filled | 8 | 7 |
| Total number of vacancies | -2 | -1 |
| **Nurse Clinicians** | | |
| Total number of positions | 33 | 30 |
| Total number of positions filled | 30 | 27 |
| Total number of vacancies | -3 | -3 |
| **Staff Nurses** | | |
| Total number of positions | 341 | 351 |
| Total number of positions filled | 361 | 382 |
| Total number of vacancies | +20 | +31 |
| **Practical Nurses** | | |
| Total number of positions | 27 | 24 |
| Total number of positions filled | 28 | 26 |
| Total number of vacancies | +1 | +2 |
| **Technical Positions** | | |
| Total number of positions | 10 | 10 |
| Total number of positions filled | 10 | 10 |
| Total number of vacancies | 0 | 0 |
| **Nursing Assistants** | | |
| Total number of positions | 67 | 61 |
| Total number of positions filled | 74* | 61** |
| Total number of vacancies | +7 | 0 |
| **Clerical** | | |
| Total number of positions | 49 | 50 |
| Total number of positions filled | 40 | 40 |
| Total number of vacancies | -9 | -10 |

*Includes 10 students in Stride Nursing Program at Marymount
**Includes 2 students in Stride Nursing Program at Marymount

ATTACHMENT III

## NURSING RESEARCH STUDIES THAT HAVE BEEN/ARE BEING DONE AT THE CLINICAL CENTER, NURSING DEPARTMENT, NIH SINCE 1975

| NAME (Investigator or Guest) | Project Title | Status of Project |
|---|---|---|
| Regina Moses | Prevention of Dry Mouth in Post-Operative Patients | Master's thesis-1979 University of Maryland<br>No publications |
| Frances Harpine | The Relationship Between Feedback from Co-worker and Considerate and Responsible Behavior of Nurses in Leadership Positions | D.N.Sc. dissertation-1975<br>Catholic University<br>No publications/Inservice given |
| Thomas Chase<br>Kathleen Roche<br>Andrea Gielen | Death Anxiety in Huntington's Disease | Clinical Center Study<br>Completed 1975<br>Publication Pending<br>Omega Journal |
| Dorothy Belling | Use of the Swivel Adaptor Aperture during Suctioning to Prevent Hypoxemia in the Mechanically Ventilated Patient | Completed 1976<br>Published - attached<br>Heart and Lung, 7:320-322<br>March-April, 1978 |
| Mildred Kadin | Quality Nursing Care | Clinical Center Study<br>Completed 1976<br>No publications/report |
| Ruth Carlsen | Job Satisfaction of Staff Registered Nurses in Team and Primary Nursing Systems | Clinical Center Study<br>Completed 1977<br>Publication Pending-<br>Manuscript Submitted 11/78 |
| Mary Ann McDonough | Attitudes of Pediatric Nurses toward Rooming-in of Patients | Master's thesis-1977<br>Catholic University<br>No publications<br>Report 1/79 |

ATTACHMENT IV

## CLINICAL CENTER RESEARCH STUDIES IN NURSING Page 2 - Continued

| NAME (Investigator or Guest) | Project Title | Status of Project |
|---|---|---|
| Susan Simmons | The Relationship of Rotating Tours and Extended Tours of Duty to Nurses' Cognitive Capacity | Master's thesis-1977<br>Catholic University<br>No publications<br>3 Brown Bag Inservice Reports |
| Freddie Grice, Emma Vogel | Effects of Body Position on Nausea and Vomiting | Approved Protocol 4/5/78<br>Data Collection |
| Candyce Echelberger | Effect of Positioning on Intraventricular Drug Distribution After Intrathecal Administration of Methotrexate | Approved Protocol 8/22/78<br>Data Collection/Analysis |
| Cass Connelly | Correlates of Compliance in Patients Being Treated for Manic Depressive Psychosis | D.N.Sc. Dissertation<br>Catholic University<br>Completed - 5/1979<br>Brown Bag - 6/28/79 |
| Amelia Jackson<br>Cynthia Schilsky<br>Florence Sato<br>Rachel Brown<br>Jill Nusbaum | The First Step in Initiating Nursing Research in a Clinical Setting | Approved Protocol 10/18/78<br>Publication pending |
| Jennifer Burks<br>Patricia Griffith<br>Kathleen McCormick | Radiation Exposure to Nursing Personnel on 7 West from Patients Receiving Diagnostic Radionuclides | Approved Protocol 12/78<br>Publication pending<br>Abstract Submitted - Accepted for Presentation 10/79<br>University of Delaware |

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ATTACHMENT IV

CLINICAL CENTER RESEARCH STUDIES IN NURSING Page 3 - Continued

| NAME (Investigator or Guest) | Project Title | Status of Project |
|---|---|---|
| Kathleen McCormick<br>Marsha Moore<br>Virginia Dodds<br>Dane Rosenbery | Correlates of Activity of Patients with Diffuse Fibrotic Lung Disease | Protocol Review/Endorsed by Nursing<br>HLBI Review pending |
| Diane Arathuzik | An Operational Definition of Suffering | Pilot Completed 2/79 |
| Tom Anderson<br>Dianne Howser<br>Audrey Barlock<br>Susan Hubbard | The Use of Transdermal Therapeutic Systems-Scopolamine in the Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy | Data Collection |
| Audrey Barlock | Nursing Management of Adriamycin Extravasation | AJN, Jan. 1979 |
| Susan Steinberg | Patient Perceptions of Quality Assurance | Protocol Review |
| Elizabeth Reisman | Nursing Involvement in Informed Consent | Literature/Protocol, Development<br>D.N.Sc. Dissertation-CU |
| Barbara Resnick | Nurses Role in Intravenous Catheter Placement | Deferred |
| Deborah Wolff | Components of Primary Nursing | Literature |
| Kathy Moorehead | Pain Intervention Techniques | Deferred |

ATTACHMENT IV

CLINICAL CENTER RESEARCH STUDIES IN NURSING Page 4 - Continued

| NAME (Investigator or Guest) | Project Title | Status of Project |
|---|---|---|
| Bernice Kraker<br>Sarah Young<br>Joan Vander Molen | Clean Catch Procedure Techniques | Deferred |
| Barbara Rollings | Assessment of Teaching Aids in Patients Receiving Blood Transfusions | Protocol Development FAES Class |
| Venida Hamilton<br>Emma Vogel<br>Patsy McCabe<br>Pauline Reed | What Patients Want to Know About Health | Tool Design |
| Juliana Rugg | An Empathy Teaching Program to Improve the Empathic Communication of Nurses | Tool Design |
| Maureen Knippen | Sleep and Mobility in Patients with Arthritis | Feasibility/Literature |
| Kathleen McCormick | Lipidemia and Blood Transfusion Reactions | Protocol Design |
| Kathleen McCormick | Determinants of Neurogenic Pulmonary Edema | Deferred |
| Jeannette Thomachewski<br>Adrienne Hope | Assessment of Antiemetics on Minors on 10 East | Deferred |
| Jean Jenkins<br>Claudia Seipp | Human Sexuality in Patients Receiving Chemotherapy | Deferred |

ATTACHMENT IV

CLINICAL CENTER RESEARCH STUDIES IN NURSING Page 5 - Continued

| NAME (Investigator or Guest) | Project Title | Status of Project |
|---|---|---|
| Audrey Barlock | Nursing Management of Adriamycin Extravasation (Animal Study) | Protocol Development (FAES) |
| Regina Moses<br>June McCalla | An Investigation of Prophylactic Oral Hygiene to Reduce Bacterial and Fungal Mouth Flora in an Effort to Diminish Oral Mucositis Subsequent to Chemotherapy | Nursing Research Review - Deferred<br>Publication pending |
| Clinical Nurse Expert Group | Therapeutic Touch | Deferred |
| Cora Ruff | Loneliness in Patients with Sickle Cell Anemia | Feasibility/Literature<br>Catholic University<br>Doctoral Student |
| Judith Schmidt | The Application of an Intervention Technique to Reduce Stress in High-Low Life | Protocol Development<br>Catholic University<br>Doctoral Student |
| Elaine Stashinko | An Investigation of Nurses' Attitudes toward Pediatric Patient Care | University of Maryland<br>Masters Student<br>Completed 5/79/no reports |
| Dale Clymer | Adult Symbiotic Behavior in Patients with Affective Disorders | Protocol Reviewed by Nursing<br>Catholic University<br>Masters Student<br>Pending NIMH Review |

ATTACHMENT IV

CLINICAL CENTER RESEARCH STUDIES IN NURSING Page 6 - Continued

| NAME (Investigator or Guest) | Project Title | Status of Project |
|---|---|---|
| Majorie Dehlinger | An Evaluation of the Computer in the Management of Nursing Care to Patients | Feasibility/Literature |
| Kathleen McCormick<br>Mary Feld<br>Mary Cornelius | Anthropometric Correlations of Mandibular Diameter to Tracheal Diameter | Feasibility/Literature<br>Protocol Design |
| Judith Wackenhut | Changes in the Behaviors of Children with Cancer from Diagnosis through Treatment | Protocol Design/Editing |
| Margaret Flanagan | Research Knowledge as Indicators of Productive Research Outcomes | Protocol Design |
| Jo Ellen Howard | Weaning Postoperative Patients from Mechanical Ventilation: Implications for the ICU Nurse | Literature/Feasibility<br>Catholic University |

Edited: June, 1979
K.M.

ATTACHMENT IV

## Nursing Department Staff in School

| Position | Full Time | Part Time | Stride Program Full Time | Upward Mobility Program |
|---|---|---|---|---|
| RN | 2* | 119** | 5*** | 1 |
| NA | | | 2**** | 2 |
| Unit Clerk | | 4 | 1**** | 2 |
| LPN | | | | 3 |
| Secretary | | 2 | 1**** | 3 |
| Clerk Typist | | | 5**** | |
| Patient Care Tech. | | 2 | | 5 |
| Inhalation Therapy Tech. | | | 1**** | |
| Total | 2 | 127 | 15 | 16 |

* 2 RNs fully funded by Nursing Department
** 98 credit courses
21 non credit courses of 40 hours or more
*** B.S. Extended Program
**** A.A.S. Program

ATTACHMENT V

## Educational Program

|  | Times Offered | Total Number of Participants | Comments |
|---|---|---|---|
| 1. Intramural |  |  |  |
| a. Orientation |  |  |  |
| Professional Nurse | 24 | 149 | Includes 6 Stride Nursing Graduates |
| Administrative Assistant | 1 | 1 |  |
| Clerk Typist | 10 | 26 |  |
| Housekeeping Aide | 1 | 1 |  |
| b. New Graduate Program | 2 | 10 | First offered 5/79 |
| c. Mandatory Review |  |  |  |
| a) Cardiopulmonary Resuscitation |  |  | Scheduled at the unit level |
| b) Fire Safety Program |  |  |  |
| 1) Fire Extinguisher Utilization | 8 | 7 | 1979 records only (incomplete) |
| 2) Fire Safety Films | 12+9* | 155+13* | Films and Evacuation Practice combined into one class 1/79 |
| 3) Evacuation Techniques | 12 | 136 |  |
| Infection Control | 2+8* | 26+15* | New Program 6/79 |
| Radiation Safety | 4+10* | 67 | *Orientation classes to which employees might attend in place of scheduled review sessions |
| d. Administration of Blood and Blood Products Course | 3 | 65 |  |
| e. Intensive Care Nursing Course | 1 | 10 | New Program 4/79 |

ATTACHMENT VI

|  | Times Offered | Total Number of Participants | Comments |
|---|---|---|---|
| f. Preceptorship | 2 | 18 | New Program 4/79 for Head Nurses, Clinical Nurse Experts, Preceptors |
| g. Nephrology |  |  |  |
| Renal I | 4 | 74 | In addition 20 independent learners |
| Renal II | 1 | 15 | New program 5/79 |
| h. Respiratory Assessment | 4 | 35 |  |
| 2. Extramural |  |  |  |
| a. Undergraduate |  |  |  |
| B.S.N. Marymount Practicum | 1 | 10 | Instructor from Marymount present during practicum for first time |
| Cancer Work - Study | 1 | 20 |  |
| Clinical Electives Program | 4 | 24 |  |
| Co-Step Program | 3 | 6 |  |
| Summer Nursing Assistant | 3 | 9 |  |
| 3. Graduate |  |  |  |
| Master's Student | 1 | 1 | Chief, Nursing Education preceptor for educational practicum |
| Foreign Nurse Program | 1 | 1 | From Royal Marsden Sutton, Surrey England |
| FAES (Graduate School at NIH) |  |  | Chief, Nursing Education coordinates nursing courses as chairperson, Nursing Department |

ATTACHMENT VI

## Continuing Education Programs in Nursing Approved by the Public Health Service Review Committee on Continuing Education in Nursing

| TITLE | CONTINUING EDUCATION UNIT |
|---|---|
| Cancer Nursing Update - 79 | 0.15 |
| Group Theory and Process | 1.6 |
| Health Education: An Essential Component of Health Care | 0.1 |
| Nephrology Nursing Course | 2.0 |
| Preceptorship and Perspective in Role Clarification | 0.2 |
| The Primary Nurse Role and The Nursing Process | 1.0 |
| Respiratory Assessment | 2.8 |
| Rheumatoid Arthritis | 0.2 |
| Suicide - The Challenge For Nurses | 0.2 |
| Continuing Education Workshop for Nurses-Nursing Research Proposal Review | .6 |
| Fifth Annual Nursing Research Symposium | .2 |
| Nursing Care Responsibilities for Patient's Receiving Blood and Blood Products | 1.6 |
| Nursing Care of the Patient with Thalassemia and Iron Overload | .15 |
| Nursing Management of the Patient on the MAI Ventilator | .2 |

10 contact hours = 1 continuing education unit

ATTACHMENT VII

REHAB. MED.

NUTRITION

OCC. MED.

OPD

PHARMACY

October 1, 1978, through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

# NUTRITION DEPARTMENT

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October 1, 1978, through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## NUTRITION DEPARTMENT

### I. DEPARTMENT MISSION AND GOALS

The Nutrition Department of the Clinical Center assumes two major responsibilities for the patients participating in the various clinical studies of the nine Institutes. These are:

1. To provide the nutritional requirements of the continuing clinical research programs and to provide the patient with support in adjusting to dietary changes essential to his condition or to the needs of the research protocol. This may require adapting food preparation and service to meet the needs of the protocol while at the same time maintaining high quality food service to all patients.

2. To provide nutritional instruction. (A) Inpatients are instructed concerning the dietary requirements of their individual research protocol. Upon discharge, if requested by the physician, a therapeutic dietary regimen is provided according to the physician's written order. (B) Outpatient nutritional instruction is given when requested by the physician.

Food is prepared in one central kitchen and distributed to each of the twelve floor kitchens from which the individual trays are served. The use of decentralized tray service provides a valuable means of meeting individual patient's needs and preferences as well as the needs of the investigators. Two specialized units, the 8th Floor Metabolic Kitchen Unit and the 2B Laminar Flow Kitchen Unit, have been in continuous operation this year. The Metabolic Kitchen Unit provides investigators from NHLBI, NIAMDD, NCI, and NICHD with services that permit them to undertake metabolic balance studies and other carefully controlled studies involving the measurement of nutritional intake. The Laminar Flow Kitchen Unit provides a food service with controls designed to reduce the high risk of infection by providing a protected environment for patients undergoing chemotherapy.

In addition, the professional staff of the Nutrition Department have been accorded a leadership role by serving as a major nutritional reference group for dietitians and physicians throughout the United States. Two Nutrition Department publications serve as standards for service throughout the United States - "A Dietetic Manual for Metabolic Kitchen Units," which describes procedures and techniques used at the Clinical Center, and "The Dietary Management of Hyperlipoproteinemia - A Handbook for Physicians and Dietitians," published by NHLBI staff in collaboration with the staff of the Nutrition Department.

Twenty-five years ago this Department was a showplace for modern hospital kitchens. After completion of the remodeling of the main kitchen in 1980, the Department will once again have the latest, most modern, up-to-date equipment.

## II. DEPARTMENT ACTIVITIES

During Fiscal Year 1979 the Nutrition Department served a total of 340,120 meals. Of these, 33,058, were classified as Category 3 and 4 type diets. These categories require professional staff participation in planning individual meals and service, which are an integral part of a clinical research study and provide the investigator with necessary nutritional information to assist with the interpretation of the data obtained. Many of the clinical research protocols implemented at the Clinical Center necessitate the control of nutrients, calories, fluids, and, in some cases, the control of the source of the food served. A sufficient number of well-qualified staff are essential to the success of these programs.

## III. MAJOR PROGRESS IN RESEARCH, SERVICE, TRAINING AND DEVELOPMENT

As indicated above, approximately 9% of the total meals served in this fiscal year were directly related to the medical research at the Clinical Center. In addition to serving three meals a day, the Nutrition Department has provided these additional services:

1. Measured and controlled fluids in conjunction with the nursing staff for an average of 58 patients each day.

2. Provided accurate measurement of all food eaten for an average of 76 patients each day. This required daily calculation of food consumption.

3. Provided control of specific nutrient intake for 40 patients each day. This required the checking back of each meal tray and replacement of the appropriate nutrient being controlled by dietary intake.

4. Provided 2,813 meals for the Laminar Flow Kitchen Unit (approx. 234 a month). Each met the Clinical Center's standards of reverse isolation for the Laminar Flow Unit.

5. Responded to an average of 125 diet changes a day.

6. Provided an average of 68 diet instructions and/or consultations per month to the outpatient studies.

Nutrition expertise has been provided to the NIH Nutrition Coordinating Committee, the NIH GAO Investigation of food service to the cancer patient at the Clinical Center and other selected hospitals, and to NCI in reviewing nutrition publications for the cancer patient.

Considerable time has been devoted to purchasing demands, market changes, and to NIH's Office of Financial Management in the handling of payment for purchases received.

Emphasis has been placed on improvement of communications within the Department and with other Departments of the Clinical Center. The Nutrition/Nursing Committee has identified some of the needs of both Departments in the area of communications.

A study has been made to evaluate the current food service standards of service and the equipment available on today's market. Equipment to improve the service of hot food has been selected, tested, and found to be satisfactory. The Finessa dispenser hot food cart and insulated soup bowl and cup will be initiated in FY 1980 along with a changeover to pyceram dishware to replace plastic dishes.

A new union agreement was negotiated with AFGE Local 2419 and became effective on December 18, 1978.

There has been continued emphasis on training for all groups within the Department. Col. Thelma Arnold, Assistant Professor, Department of Biochemistry, Uniformed Services University of the Health Sciences, has served as a consultant to the staff of the Patient Dietetic Service. Since December 1978 she spent 8 hours each month in this capacity.

Each month two or three staff meetings have been scheduled for the professional staff. Recognized speakers in their fields have been invited to these meetings which provided the dietitians registration credit in the amount of 1-2 hours each month.

Top priority has been given to the provision of outside training experiences for the staff. Some of the most significant are listed below:

1. Six staff members continue to attend Adult Education classes and 1-3 staff members attend Upward Mobility College classes
2. The Deputy Kitchen Manager attended Motivational Dynamics as part of the Leadership Training program
3. The Chief, Nutrition Department, participated in a seminar for Clinical Center deparment heads entitled "Managing Interpersonal Relationships"
4. Three administrative dietitians and the kitchen manager staff attended the "Spotlight on Safety" seminar in October
5. One dietitian attended a workshop entitled "Coronary Atherosclerosis - A Review of Nutritional Factors in Prevention and Management," conducted by The American Heart Association
6. Three dietitians attended the annual meeting of The American Dietetic Association

7. One dietitian attended a two-day meeting on "Nutritional Care of the Hospitalized Patient - A Team Concept," sponsored by The American Society for Parenteral and Enteral Nutrition

8. One dietitian attended a two-day seminar entitled "Nutrition and Gastroenterology" sponsored by The Institute of Human Nutrition, Columbia University

## IV. FUTURE OBJECTIVES

During the year a Nutrition Department Goals Committee was established. This committee is comprised of the Chief and Deputy Chief, Nutrition Department, and the two service chiefs. The goals set by the committee for FY 1980 are as follows:

1. Complete the remodeling of the main kitchen and re-establish quality-controlled decentralized food service for the patients of the Clinical Center

2. Revise current diet instruction materials and procedures to provide a sound basis for diet instruction service in the new ACRF Building

3. Re-establish an extensive in-service training program for the nonprofessional staff in the Patient Dietetic Service

4. Revise the diet manual

5. Revise the food portion manual

6. Initiate a three-week cycle menu. Cost savings are anticipated by reducing the number of food items to be purchased and the number of menus to be printed (reducing typing time and paper).

## V. PROBLEMS

The major problems of the Nutrition Department have centered around the failure of the contractor (hired to remodel the main kitchen) to do any work during the first half of this fiscal year. Much of the equipment installed during the latter part of the fiscal year did not meet specifications. This stalling has placed an unnecessary burden on the Food Production Service staff and has contributed to poor morale, absentee problems, and in some cases, the quality of the food served to the patients.

Budget problems and restrictions on employment necessitated a number of adjustments in Department procedures.

Inflation continues to influence increases in cost of food, supplies, and equipment. Insufficient funds ($6,000) were allocated for equipment within this 25-year old Department. The inability to replace some of the equipment in the floor kitchens handicaps the units periodically. The funds expended by the Nutrition Department were as follows:

| | |
|---|---|
| Personnel | $2,545,435 |
| Food | 747,605 |
| Equipment and Supplies | 110,892 |
| Training and Travel | 6,966 |
| TOTAL | $3,410,898 |

These figures reflect increased food prices and decreased personnel costs due to reduced positions and some curtailment of overtime.

The Clinical Center experienced two major crises during this year - the paralyzing snowstorm of February 19, 1979, a Government holiday, and a fire on 9-West on April 21, 1979, which necessitated the evacuation of 24 nursing units. The Nutrition Department was able to provide complete services on February 19 for the total day with a very limited staff and volunteer assistance. The fire occurred in mid-afternoon and upon their return to the nursing units, patients were served a hot dinner meal by the Nutrition Department staff.

REHAB. MED.

SOCIAL WORK

OCC. MED.

OPD

PHARMACY

October 1, 1978,through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

OFFICE OF OCCUPATIONAL MEDICINE

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October 1, 1978, through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## OFFICE OF OCCUPATIONAL MEDICINE

### Department Missions and Goals

The Office of Occupational Medicine through the Occupational Medical Service provides an extensive medical program for all employees of the National Instituees of Health which includes all elements of the Federal Employee Occupational Health Program as specified by Executive and HEW Directives.

The Occupational Medical Service is administratively accountable to the Chief, Office of Occupational Medicine, CC, who also serves as the Occupational Health Officer, NIH. National Health Services, Inc., was selected through competitive bidding as the contractor for the operation of the Occupational Medical Service at NIH beginning July 1, 1974. In carrying out its responsibilities, the Occupational Medical Service works closely the the Associate Director for Environmental Health and Safety, DRS, the Director, Office of Research Safety, NCI, and NIH Institute Clinical Directors.

The Occupational Medical Service is responsible for maintaining essential services and facilities to provide emergency treatment for on-the-job illness or injury of employees; provides health education and preventive medical programs to make employees aware of the importance of maintaining good health; advises management and employees in resolving work related health problems; assists management in evaluating handicapped individuals in terms of specific job assignments; develops and executes a comprehensive mental health program for NIH, including alcoholism and drug abuse conseling; and develops medical surveillance programs designed to minimize environmental health hazards.

The Occupational Medical Service's goal is to assure that employees are able to perform their duties without hazard to themselves or others; to offer job assignments in relation to medical fitness; to provide preventive medical services to assist employees in meeting their health needs; to prevent adverse effects of hazards in the work environment; and to provide clinical consultation for occupational diseases for employees and Clinical Center patients at the request of Institute physicians.

### Department Activities

A. Workload
Statistics in Table I have been prepared for October 1, 1978, through September 30, 1979. Statistics used for the last quarter of FY-79 are those from the last quarter of FY-78, since statistics for the end of FY-79 are not yet available. There has been an increase in the total number of visits since the Main Health Unit was temporarily moved from Bldg. 10 to Bldg. 31.

B. Personnel

Following four years as OMS Medical Director, Dr. Robert J. Brandt resigned September 1978 to accept a position with a consulting firm in the area. Dr. Barbara Wasserman, Assistant Medical Director was promoted to Acting Medical Director until March 1979 when Dr. Julio C. Rivera was appointed Medical Director. As required in the contract, Dr. Rivera is certified in occupational medicine by the American Board of Preventive Medicine.

Mrs. Anne D. Foster, OMS Chief Nurse since 1974 resigned in October 1978 due to a medical condition. Mrs. Mary McKnight, who has worked at OMS for four years as Staff Nurse and recently as Assistant Chief Nurse was promoted to Acting Chief Nurse. After one year of satisfactory supervisory experience she will be promoted to Chief, Nurse, OMS.

On July 1, 1979, a pay raise was given to all nurses to make their salaries competitive with Civil Service Occupational Health Nurses. This action was taken to improve recruiting and retention of National Health Service, Inc. staff nurses.

C. Evening Clinic

In March 1979 Dr. H. Randall Hicks was assigned full-time to the evening clinic at Bldg. 10. Dr. Hicks and his staff nurse, Ms. Tara McCarthy, developed a publicity program including an open house, to increase utilization of this clinic. Visits to the evening clinic have increased by about 40-50%. Educational preventive medicine programs are also routinely presented.

D. Main Health Unit, Bldg. 31

The inadequate soundproofing problem at this unit continues uncorrected. This problem seriously interferes with the daily work of the psychiatrist and mental health counselors. The physical limitations and functioning capabilities of the Bldg. 31 Emergency Room were re-evaluated. The number of stretchers was reduced from three to two after it was found that there was inadequate space for personnel to work effectively. In recognizing the limitations imposed by our physical separation from Clinical Center support systems such as radiology and Clinical Center cardiac arrest team, a number of improvements were made. These included: improved communication equipment and guidelines between OMS and NIH ambulances and revised emergency room guidelines for Bldg. 31.

The shortage of examining rooms with tables at this Unit creates a serious problem which at times leads to a line of physicians and nurses waiting to use the two existing rooms. Patient's waiting time is also increased due to lack of examining tables. Three examining tables will be ordered to alleviate this situation.

E. Health Unit, Bldg. 13

Recently this Health Unit was remodeled and its size doubled. Expansion included: an additional office, expanded bed space, additional special facilities for treatment and examination, and an audiometric booth was installed.

### F. Administrative Improvements

The OMS organization was restructured to reduce the number of OMS staff reporting directly to the Medical Director, to emphasize the daily clinical responsibilities of the Assistant Chief Nurse and the Assistant Medical Director, and to give adequate recognition to the position of the Office Manager who has primary responsibility for the daily administrative operation of the OMS health units.

An extensive revision and updating of the OMS Operation Manual was completed and is being typed. Position descriptions were prepared for the OMS staff.

A Central Supply inventory form which will allow more accurate estimates of medical supply needs over the year was developed for use in all the health units. Maintenance of an accurate inventory should also minimize the accumulation of outdated supplies and reduce the number of trips by OMS staff to the Clinical Center for supplies.

In an effort to enhance NIH-OMS working relationships, the Medical Director arranged various meetings with NIH management to acquaint them in detail with the Occupational Medical Service Program and also to get ideas on how OMS might better serve the NIH employees. Conferences were held with several BID Directors and Personnel Officers. In addition, the Medical Director on two occasions addressed the joint meeting of all BID Personnel Officers.

## Major Progress in Research, Services, Training, and Development

### A. Research

On March 2, 1978, the Occupational Medical Service Operations Research Advisory Committee selected five items for top priority to be reviewed as future objectives for OMS. These objectives were reviewed with the Committee at their meeting March 5, 1979. An update of these objectives follows:

1. Expanding epidemiological opportunities in occupational medicine utilizing the stable employee population.

   A report entitled, "Surveillance of Hepatitis-B Exposures by Accidental Innoculation" was prepared by an OMS physician and submitted to the Clinical Center Safety Committee. After reviewing the results and recommendations, the Safety Committee, working with CC Information Office staff, initiated several articles in the Clinical Center Close-up to inform employees of the risks associated with needlestick injuries. In addition, the Committee formed a working sub-committee to study puncture wounds occurring in high risk employee groups (nurses, laboratory technicians, and housekeepers) and develop approaches to reduce hazardous conditions. An OMS staff nurse is a member of the sub-committee.

The OMS medical staff reviewed the current OMS program for monitoring communicable diseases in NIH employees and decided that a new approach should be developed, particularly for those employees who have patient care contact. OMS physicians are working with the Chairman of the Clinical Center Infection Control Committee, and the new Director, Hospital Infection Prevention Program and two nurse epidemiologists to develop a monitoring program that is medically appropriate, meets JCAH requirements, and provides a useful working tool for departments in the Clinical Center.

OMS and NCI personnel agreed to undertake a joint review and evaluation of the Special Viral Containment Program (SVCP). The SVCP program, which was established to provide health surveillance for a group of NCI employees with job-related exposures to oncongenic viruses and chemical carcinogens, provides for periodic medical evaluations by the OMS staff. The review of the eight year old program includes reviewing about 200 charts of employees with abnormal laboratory results to determine if there are any laboratory parameters that might serve as useful markers in a health surveillance protocol for employees working with oncogenic viruses or chemical carcinogens.

The OMS High Blood Pressure Program was very active during this year. Screening was performed on 5700 employees at 27 sites on the NIH reservation and in the Bethesda, Baltimore, and Northern Virginia areas between May and November 1978. Results showed that 85% had normal blood pressure; the remainder had borderline or high blood pressure. All employees in the latter category were followed and referred for further evaluation if indicated. Monitoring and education services for hypertensive employees is offered at all OMS Health Units and at selected sites including the National Library of Medicine, Blair Building, and NCI Bldgs. 35, 36 and 37. An extensive screening and follow-up program was conducted during May 1979, the High Blood Pressure Month.

2. Refining health surveillance methodology as related to specific occupational disease hazards existing at NIH.

Significant effort was expended in continuing the periodic surveillance examination for NIH employees working with oncogenic viruses, chemical carcinogens, and recombinant DNA. The animal handlers examination protocol was revised, and new protocols were developed for workers exposed to asbestos and lasers. Active surveillance programs are conducted for clinical and laboratory workers and animal handlers exposed to tuberculosis and hepatitis. The rubella screening program for all female employees of the child bearing age has been widely accepted, and during the second quarter FY-79, which included summer hiring, 259 employees were screened.

In addition to the chemical or evnironmental surveillance discussed above, the surveillance program for NIH firemen and guards was expanded. The program includes assessment for cardiac risk factors as well as EKG stress test and pulmonary function tests. An outside contractor provides a physical conditioning program and the Clinical Center Nutrition Department provides dietary counselling to employees who are overweight or hyperlipidemic. A psychiatric screening has been added to this protocol for use with a new group of NIH policemen who will be carrying fire arms.

3. Continuing evaluation of the OMS Medical Record System to assure that specific occupational health needs of the NIH are being met.

   The filing system for the OMS health records was changed to permit the gradual assimilation of records of all NIH employees under a single system. A major improvement reported by the clerical staff is faster retrieval of records needed for daily patient care.

   The OMS staff has revised the "Preferential Parking" form to include additional information by the employee's private physician. The goal is to speed OMS's processing of preferential parking requests and limit the number of calls to private physicians for additional information.

   The staffs of the OMS and the Clinical Center Nutrition Department have discussed improved ways of providing care for and monitoring employees with occupational injuries or illnesses. The "blue sheet" which provides information to the supervisor on the employee following a visit to the OMS Health Unit, was revised with the assistance of the Nutrition Department in order to clarify the disposition plan for employees.

   An overprint in the health record progress notes was prepared for light duty pre-employment examinations. Time taken by the nurses in reviewing the employee's history has been shortened considerably.

   Stricter rules were established for the release of health records information related to work injuries, which cannot be released without permission from the Federal Office of Workers Compensation Programs. A form letter was prepared advising employees of their right to receive health record information and where to write for the authorization for release of the information.

   A review of animal handlers' health records was conducted to verify accuracy of the records and to determine if there was need for further medical surveillance.

4. Steps needed to improve liaison with the Environmental Safety Branch, DRS, and other environmental health and safety programs at NIH to provide more complete health hazard exposure data for effective health surveillance.

   OMS/ESB Liaison. Progress in the joint effort by OMS/ESB to improve health surveillance has been slow. This has been attributed to the reorganization process in ESB. Environmental surveys are not routinely sent to OMS, but sometimes environmental exposure data is sent to OMS in cases of personnel exposures requiring medical evaluation. Some recent examples of joint efforts are: exposure to betapropiolactone, ethylene oxide, asbestos, and cyanide gas. The monthly meeting of OMS/ESB continues to be a forum to exchange information about areas of joint interest. During recent meetings the following programs were planned: indentification and medical surveillance of asbestos and laser workers; Q-fever survey of animal handlers and sheep herd at Poolesville; and modifications to the periodic medical surveillance recall list produced by the Computer Division.

Radiation Safety Branch. The new OMS Medical Director had a briefing and tour of the Radiation Safety Branch. Being experienced in radiation health, he was able to work closely with radiation safety personnel in two cases of alleged overexposure to ionizing radiation. As a result of a cooperative effort and early intervention, there were no instances in which workers' compensation claims were filed erroneously.

NCI Research Safety Office. The OMS Medical Director and the NIH Occupational Health Officer met with the Director, NCI Research Safety Office and the Director, NCI Office of Biohazards Safety, Viral Oncology Program to discuss the ongoing review of charts of employees working with oncogenic viruses and chemical carcinogens. They proposed to extend the programs to cover about 2000 workers.

Clinical Center Infection Control Committee. In addition to OMS routine participation in this Committee, separate working meetings were held with the Committee Chairman and the Clinical Center nurse epidemiologists to discuss OMS surveillance protocols. Subjects discussed included: tuberculosis, hepatitis-B, varicella, needle stick injuries, and skin and wound infection.

Clinical Center Safety Committee. OMS personnel have been active in the following subcommittees: the Needle Stick Subcommittee for the treatment and report of needle stick injuries among nurisng personnel. The OMS Medical Director provides advisory services to the subcommittee assigned with revising the Clinical Center Disaster Plan.

NIH Biosafety Committee. OMS continues to work closely with this Committee and assisted in the recent revision of NIH Manual Issuance 3031-1 - Control of Certain Hazardous and Potentially Hazardous Microbiological Agents in Intramural Research.

5. Program Evaluation

On May 31, and June 5, 1979, the Vice President for Government Operations, National Health Services, Inc. conducted an audit of the OMS operations at its temporary facilities in Bldg. 31. Suggestions were made to improve the flow of patients and the working conditions at this crowded and inconveniently laid out Health Unit. With the temporary relocation of the main Health Unit from Bg.10 to Bg. 31 there was a loss of daily professional contact with clinical associates and other investigators. Not as many employees are referred to various on-going studies and clinical consultations are more difficult to obtain. The Quality Assurance Review conducted in May 1978 by a joint private industry and government committee was reported in last year's annual report.

## B. Services

### 1. Employee Assistance Program

The Employee Assistance Program, developed and expanded from the Alcoholism and Drug Abuse Program, was staffed during this reporting period by one psychiatrist working half-time and two full-time mental health counselors.

A pamphlet describing the services of the Employee Assistance Program was developed and distributed to all NIH employees in October 1978, along with a letter of support from the Director of NIH. As a result of this excellent pamphlet, the Employee Assistance Program has noted an encouraging upswing in the number of NIH employees and supervisors utilizing the program.

The main thrust of the program continues to be a concentrated effort to penetrate the NIH population, specifically, higher grade employees and female employees with addiction problems. Mental health counselors are available by appointment to see evening shift employees. In addition they visit regularly the Westwood Bldg. and the Poolesville Animal Facility. In-house programs include group therapy for alcoholics that meet twice a week, bi-weekly AA meetings, weekly Alanon meetings, and a weekly women's therapy group.

A new "Stop Smoking" program was initiated in April and is being offered on an almost continuous basis in the form of five weeks of bi-weekly meetings.

In addition, seminars, workshops, and movies are presented regularly to NIH employees. During calendar year 1978, 178 new employees were counselled. From January to March 1979 there were 64 employees counselled. Each employee was seen between one to four times before a decision about referral to community resources was made. Many of the individuals originally counselled return for occasional consultation, assistance in a crisis, or reporting on progress.

2. Although other progress in OMS services is described under "Progress in Research," OMS is service oriented and its research is directed towards setting working objectives and problem solving.

## C. Training and Development

1. Employees Health Education

This is a very active program at NIH, and some of its significant accomplishments included: revision of the employee's information pamphlet "Key to Your Health"; assembling and distributing health education pamphlets to the Health Units; multiple presentations by the mental health counselors on "Stress and Coping," "Loss and Grief," "Relaxation Techniques," "Employee Assistance Program Awareness," and "Troubled Employees"; multiple presentations of the following movies: "The Dryden File," "Smoking and How to Stop," "Breast Cancer, Where We Are," "Loser's Club" (weight reduction) and "Skin Cancer Prevention"; presentations were given to shop employees on hearing conservation and asbestos exposure. OMS physicians participate in regularly scheduled seminars "Spotlight on Safety" and "Introduction to Supervision". At these seminars an overview of the Occupational Medical Service is presented.

An action plan was submitted to the NIH Occupational Health Officer in November 1978 proposing OMS become involved in helping NIH employees acquire CPR skills. This involvement includes the implementation of CPR training classes, identification of NIH employees who are CPR instructors with certification by the Montgomery County Affiliate Chapter of the American Heart Association, identification of NIH buildings where CPR instruction has not been implemented, encouragement of NIH employees within their Institutes to organize their own CPR classes, and establishment of an active list of community resources where NIH employees may attend CPR classes outside of NIH. A total of 754 employees were certified in CPR at NIH. Sixty-five were certified during the third quarter FY-79.

2. Staff In-Service and Out-Service Education and Training

A formal five day orientation program for new nurses was established and implemented in March 1979 utilizing physician and other key personnel as resources for instruction.

An OMS nurse in-service program was initiated in November 1978 and has been presented by the OMS physicians. The goals of the program are to provide the nurses with formal instruction in areas particularly relevant to occupational health and to help them assume a more independent role as health care providers. Eighteen different topics were presented until May 1979 when a CPR re-certification course was started. Five nurses completed the re-certification course in Basic CPR which lasted until July 1979. The Chief Nurse completed a course on "Physical Assessment in Cardiac Disease."

The employee assistance staff attended the following work-related programs: Workshop on "Sexuality and the Alcoholic" by the Association of Labor-Management Administrators and Consultants on Alcoholism (ALMACA); a seminar at Georgetown University on "Family Systems," an approach to and treatment of alcoholics; AA workshop on "Alcoholism in the Workplace"; a workshop in "The Family Unit: As an Aid in the Recovery of the Alcoholic"; a workshop on the "Relationships of the Professional Counselor" with Alcoholics Anonymous. This summer both counselors attended refresher courses in mental health and counseling. The staff psychiatrist attended a refresher course in psychiatry at Georgetown University in preparation of her specialty Boards.

Physician participation in continuing education activities included attendance at the following: Regional meeting of the American College of Physicians in Williamsburg, Va.; Symposium on Emergency Medicine at the University of California in San Diego, Ca.; Ophthalmology course at Fairfax Hospital, Va.; NIH continuing education courses in Toxicology and Endocrinology; American Occupational Health Conference, Anaheim, Ca.; Advanced Cardiac Life Support at George Washington Univ. Hospital, Washington, D. C.; Basic Cardiopulmonary Resuscitation and Advanced Cardiac Life Support at the Aerospace Medical Association meeting in Washington, D. C.; Seminar on Stress at the Workplace at the D.C. Medical Society; Primary Care in an Office Setting at Harvard Medical School, Boston, Mass.; and participation at workshops at the meeting of the Institutional Biosafety Committee in Reston, Va. The Medical Director and the Assistant Medical Director attended the NIH course on Radiation Safety in the Laboratory.

An occupational health technician was certified as an Industrial Hearing Conservationist by the Washington Hearing and Speech Society. She also completed nursing courses in anatomy and physiology at Prince George's Community College. Another health technician took courses in Parasitology and EKG interpretation at Georgetown University.

## IV. Future Objectives Directed Toward Meeting Goals

In October 1978 a meeting was held with the Director, Clinical Center, to review the Quality Assurance Report and to propose goals and objectives for OMS based on program elements outlined in the contract section "Measures of Effectiveness." These elements are: emergency care, occupational health surveillance, preventive medical programs, alcoholism and mental health counselling, and administration. With the concurrence of the NIH Occupational Health Officer and the Clinical Center Director the following goals and objectives were established for the next two years.

a. Upgrade emergency care provided in OMS Health Units
b. Improve joint health surveillance efforts by OMS and Environmental Safety Branch.
c. Develop approaches to enchancing preventive health care for employees.
d. Analyze Employee Assistance Program's outreach efforts.
e. Initiate changes in administrative organization to facilitate OMS operations.
f. Increase OMS staff interaction with Personnel Officers.
g. Enhance professional role of OMS nurses.
h. Make modifications in physical structure of Bldg. 31 Health Unit.
i. Facilitate patient flow in Bldg. 31 Health Unit.

## SELECTED WORKLOAD STATISTICS, OCTOBER 1978 - SEPTEMBER 1979

| | Number of Visits | Average Monthly Frequency | Precent of Workload |
|---|---|---|---|
| Preventive Medicine Visits | 24,307* | 2,026 | 65 |
| Personal Visits | 8,373 | 698 | 22 |
| Occupational Injuries | 3,156 | 263 | 9 |
| Occupational Diseases | 1,577 | 131 | 4 |
| Total Visits | 37,413 | 3,118 | 100 |

* Includes 1880 visits for Employee Assistance Program

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CLINICAL CENTER

OUTPATIENT DEPARTMENT

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OUTPATIENT DEPARTMENT

## PROGRAM OBJECTIVES

The mission of the Outpatient Department is to assist the professional members of the Clinical Center staff to provide excellence in patient care. The Department's goal is to provide effective and convenient settings, and expeditious and comprehensive service to Clinical Center patients.

The Outpatient Department is made up of six sections: Admissions, the Clinics, the Patient Travel Office; Special Ambulatory Care Program; Local Transportation; and the Messenger and Escort Service. Each section provides special services to meet specific kinds of patient needs.

The following are the individual objectives for each section, which individually and collectively meet the overall objectives of the Department.

Admissions - The objective of this section is to admit both the inpatient and the outpatient in the most expeditious manner possible, ensuring that all information received and transcribed is accurate.

The Clinics - This section provides a setting in which physicians are able to conduct examinations and/or treatments of ambulatory patients on a timely basis, with assistance from other members of the Clinical Center staff.

The Patient Travel Office - This section provides and arranges transportation to and from the Clinical Center, taking into consideration the patients' medical and personal needs, comfort, and care with the least inconvenience to the patients.

Special Ambulatory Care Program - The objectives of this program is to offer participating Institutes and physicians a method of treating ambulatory patients, not living within commuting distance, on an outpatient basis. The patients are housed in a nearby motel and provided transportation to and from the Clinical Center for treatment.

Local Transportation - The objective of this section is to provide essential transportation for patients when the patient cannot provide his own. This includes transportation to and from the air, train, and bus terminals, special car and driver service for debilitated patients, and ambulance service for those patients needing more technical care.

Messenger and Escort Service - This section's objective is to transport patients and specimens expeditiously, always mindful of the necessary safety measures to be taken during the transportation.

DEPARTMENT ACTIVITIES

The following departmental activities are designed to meet the overall objectives of the Department as well as those of the individual sections to provide the support necessary for the highest quality patient care:

1. To maintain the maximum productivity of the employees within the Department

2. To refine the centralized appointment system so that more of our patients are seen at individual times rather than during a block of time

3. To continue to improve the supply system for the Clinics

4. To increase the number of patients preadmitted to the Clinical Center so that the patients are required to spend less time in the Admissions Office

5. To train the staff in the art of public relations and other related activities

6. To begin to reorganize the Patient Travel Office's procedures and policies to more effectively handle the ever increasing load of patient and Clinical Center employee travel

7. To orient the Institute physicians to the Outpatient Department

8. To effectively reduce the money spent on travel and the Special Ambulatory Care Program, without curtailing patient care

9. To find a more effective, cost saving device for transporting patients to and from National and Dulles Airports

10. To find solutions to solve problems between Medical Records Department and the Admissions Section

11. To better utilize the preadmission system

12. To study the implementation of the Bed Allocation System

13. To expedite the delivery of emergency medications to inpatients

14. To have all Transportation Section personnel complete the Emergency Medical Technician Course and the Cardiopulmonary Resuscitation Course

15. To establish a better system for transporting patients by taxi

16. To acquire an additional wheelchair van

17. To complete renovations of the Outpatient Department and relocate additional ancillary services to the Clinics in order to effectively utilize physician and patient time.

PROGRESS ACHIEVED

1. Some of the training programs to improve the output of work of the various employees of the Department are: inservice training sessions, participative management, and individual counseling sessions. This process is an indefinite one, as it is difficult to place limitations on it if it is to be successful.

2. The centralized appointment system has been implemented for all the Clinics. We have refined individual Clinics from block appointments to individual appointment times for the patients. There has been much success in switching the appointments for the Clinics from block times to individual times. Approximately 95% of the Clinics are utilizing individual times.

3. The staff for stocking the Clinics has been hired and have been cross-trained in all the Clinics. The program has been enlarged to encompass the handling of the patients' baggage (both inpatient and outpatient). A list of supplies used by the Clinics has been given to the Central Sterile Supply to be programmed for the Medical Information System. This list includes the number of items and their allocation by room and Clinic. The policy and procedure manual has been completed.

4. All patients are pre-admitted upon receipt of the Admissions Request Form before the patient actually arrives at the Clinical Center. This process effectively reduces the patients' time in the Admissions Section. By pre-admitting the patients, we are able to make the patient record available to the physician so that he can enter orders in the Medical Information System prior to the admission of the patient to the Clinical Center.

5. Many of the employees of the Outpatient Department participated in a seminar on Death and Dying.

6. The study of the Patient Travel Office is completed. As a result, new, more economic procedures and policies were initiated.

7. The physicians of the various Institutes were oriented by the supervisors of the Special Ambulatory Care Program, Patient Travel, Admissions Section and Clinics. This is an ongoing program for all new Clinical Center Associates.

8. The Special Ambulatory Care Program contract with United Inn of America was re-negotiated. One of the measures taken to reduce monies spent was to decrease the number of guardians (escorts) of patients transported to the Clinical Center and placed on the Special Ambulatory Care Program.

In addition, other measures were taken to more strictly enforce Patient Travel and Special Ambulatory Care Program regulations.

9. A limousine service to transport Clinical Center patients to and from National and Dulles Airports on a scheduled basis was begun in mid-April on a trial basis. This should save considerable money over the metered taxi fares. Also, this service can be utilized by employees on a space available basis.

10. A closer relationship with the Medical Records Department has been developed by establishing a committee which meets every Friday to discuss problems between Admissions and Medical Records and arrive at solutions to these problems.

11. The Admissions Section worked closely with several Institute branches, giving them a better understanding of the pre-admission process which has enhanced cooperation and increased the number of planned admission requests.

12. The Bed Allocation Program is to be utilized to admit patients (Case Category I), to other nursing units on a more formal basis.

13. The Messenger and Escort Service collaborated with Pharmacy to facilitate delivery of emergency medication to inpatients.

14. One of the drivers completed the Emergency Medical Technician - Ambulance course in September, 1979. All drivers have successfully completed the Cardiopulmonary Resuscitation Course, as have other staff members.

15. Cab service for Clinical Center patients was re-negotiated from a sole source basis to four taxi contracts which allows better service to patients.

16. A new wheelchair van was purchased which has proven most beneficial because of the large number of requests for transporting wheelchair-bound patients. The new van requires less staff to attend the patient.

17. The renovations of the Outpatient Department have been completed, with much tolerance both by patients and staff. The following changes have been accomplished:

a. Old North and East Clinics both closed permanently

b. New East Clinic, located in South Corridor behind the Reception Desk was completed and opened early October

c. South Clinic renovated with the addition of eight (8) examining rooms, which includes facilities for the newly formed ENT Clinic and Mental Health Clinic

d. Admissions Section was moved from its temporary quarters on the fourth floor to the Main Lobby

e. Messenger and Escort Service was located from the thirteenth floor to the first floor

f. The Phlebotomy Unit was moved from their location on 1D to a more spacious area on the North Corridor, first floor

g. The Fingerstick Unit was relocated from West Wing Clinic to the North Corridor with the Phlebotomy Unit

h. A Satellite X-Ray Unit has been established on the first floor, North Corridor

i. The Pulmonary Function Unit has been relocated the the first floor, North Corridor

j. The Travel Office was relocated from South Corridor to the North Corridor, giving the Pharmacy Department additional space

k. The Special Ambulatory Care Program office was relocated from 1D to the North Corridor, first floor

l. The Appointment Desk was renovated, allowing a more spacious area

m. The Nutrition Clinic was established on the first floor, North Corridor

n. The Audiology Clinic was established in West Wing Clinic.

## OTHER ACTIVITIES

1. A study of the Clinic Section was completed to expedite both patient and paperwork through the Clinical Center's Departments.

2. The Chief, Outpatient Department, is a member of the Executive Medical Information System Committee, which meets on a weekly basis to discuss problems and make plans for the Outpatient Department Medical Information System.

## PLANS

1. To further expand the duties and assignments of the Messenger and Escort Service.

2. To continue to train employees of the Outpatient Department in public relations and other related areas.

3. To continue to define and refine the Outpatient Department program for stocking Clinics.

4. To send the remaining drivers of the Local Transportation Unit to Emergency Medical Technician - Ambulance course.

5. To develop a new system of procedures for the Local Transportation Unit.

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6. To evaluate the new shuttle service for cost and service on an on-going basis.

7. To acquire an additional wheelchair van to provide more service.

8. To continue reorganization of the Clinic Section in preparation for the Medical Information System.

9. To begin to develop policies and procedures for the mini Central Service Research Center (CRSC) now located on the first floor of the Clinical Center in preparation for the larger CRSC located in the Ambulatory Care Research Facility.

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## I. MISSION AND GOAL

The primary mission of the Clinical Center Pharmacy Department is to provide comprehensive, properly coordinated pharmaceutical services of the highest quality to the patients and staff of the Clinical Center.

The Department's goal is to meet the needs of the diagnostic and therapeutic departments, the nursing service, the medical staff, and the hospital as a whole to ensure better patient care.

To accomplish its mission and goal, the Pharmacy Department is also engaged in pharmaceutical development, training, and research.

The Pharmacy Department consists of the Pharmacy, Pharmaceutical Development, Central Sterile Supply Services and the Office of the Chief. The Pharmacy Service interprets and transcribes medication orders, and monitors and dispenses all medications ordered for patients in the Clinical Center. This Service fulfills these responsibilities by dispensing unit doses (individually packaged and labeled dispensing doses) to each patient; it fills drug orders for patients on pass, discharged, and outpatients. This Service prepares all intravenous (13,000 per month) additive solutions ordered for inpatients and outpatients; it fills drug requisitions for clinics and other patient care areas not on unit dose system; it compounds and packages products not available commercially and maintains all investigational drug dispensing records. The Pharmacy Service also provides drug information and clinical services for physicians and nurses.

The Pharmaceutical Development Service (PDS) is responsible for the registration and control of all investigational drugs used for patients in the Clinical Center. The PDS also develops, formulates, and assays many investigational drug products used by physicians in their clinical research studies. The Service also supports physicians with such services as in vitro and in vivo drug identity and analyses, setting up single- and double-blind studies, maintaining disposition records, submitting manufacturing data in support of an IND to the FDA, and providing investigational drug information.

Central Sterile Supply Service (CSSS) provides clean and sterile supplies used in patient care. This Service decontaminates, processes, assembles, sterilizes, and issues a variety of packs, trays, sets, instruments, and utensils. It also procures, stocks, and issues many clean and sterile preprocessed disposable items to patient care areas and uses a 24-hour mobile exchange cart delivery system to deliver these supplies.

The Office of the Chief provides overall policy and direction to the services and centralized procurement of approximately $4,000,000 worth of drugs and sterile supplies.

## II. DEPARTMENT ACTIVITIES

As seen in Table I, unit doses dispensed increased from 594,753 to 723,108 (22%), sterile items compounded by the Intravenous Additive Unit (IVAU) decreased from 5,711 to 3,918 (32%), outpatient prescriptions dispensed decreased from 83,451 to 77,945 (7%), and IV admixtures prepared decreased from 163,978 to 151,158 (8%).

The entire pharmacy office, along with secretarial staff, was relocated to the South Corridor area outside of the main pharmacy in Room 1S-257. This permitted the space formerly occupied by the Office of the Chief to be converted to production work area with an addition of 400 sq. feet which facilitated expansion of the unit dose and inpatient dispensing areas, and put them in close proximity to the dumbwaiters and pickup and delivery systems. Work counters were enlarged and work modules rearranged to provide better work flow in this area. Also, the former pharmacy office anteroom was walled off and became an inpatient dispensing area.

As seen in Table I, the total number of units formulated, developed, and issued by the Pharmaceutical Development Service increased from 750,740 to 937,858 (24.9%); the number of requests for service increased from 1,132 to 1,152 (1.8%); and investigational drugs registered increased from 613 to 772 (25.9%).

As seen in Table I, requisitions filled by Central Sterile Supply Service remained unchanged, items issued increased 49%, and trays and sets prepared increased 9%.

## III. MAJOR PROGRESS IN SERVICES, TRAINING, DEVELOPMENT AND RESEARCH

### Service

The Pharmacy Service's IVAU established a system for the uniform preparation of certain cardiac drugs (dopamine, lidocaine, etc.) used in intravenous drips for the 6 West Intensive Care Unit. A chart, based on exact drug concentration of the admixed bottle (in mcg/ml), was developed as a guide for use on the nursing unit and in the pharmacy. In addition, MIS screens were developed to facilitate order entry of these IV medications.

As a result of several new NCI protocols involving the administration of cancer chemotherapeutic agents in peritoneal dialysis solutions, the IVAU became involved in the preparation of these solutions. Also, studies were performed by the Pharmaceutical Development Service to assure the compatibility and stability of these chemotherapeutic agents in the dialysate solutions.

A satellite intravenous admixture unit was established in the Outpatient Clinic, South Wing. Special policies and procedures were developed, and a two week pilot study was completed before initiating the service. The main objective of the service was to have pharmacists admix, in a controlled sterile environment using a laminar flow hood, parenteral cancer chemotherapy for administration to NCI Medicine Branch clinic patients. The pharmacist also provides protocol and drug therapy monitoring service for these patients.

Comprehensive pharmaceutical service was provided to the new 10D, Medical Intensive Care Unit, with special arrangements for delivery of drugs, intravenous admixtures, and central sterile supplies.

The PDS obtained 180 square feet from the adjoining Central Sterile Supply Service to provide space for a clinical pharmacokinetics laboratory. This laboratory has evaluated a semi-automated immunoassay method for determining serum levels of various drugs. Using this method, the PDS began providing a new service - the determination of serum of CSF levels of methotrexate for NCI patients in the Clinical Center.

The Central Sterile Supply Service improved its service by extending hours of operation until midnight on weekdays and until 8:30 p.m. on Saturdays, Sundays, and holidays, with no additional increase in staff. This Service took an active part in the Safety Committee in developing policies and procedures for medical devices.

Following JCAH recommendations, CSSS has begun to assume the responsibility for centralized sterilization for the various patient care areas in the Clinical Center.

CSSS made major modifications to the quality control system for sterilization. This incorporates the Hospital Infections Committee spore testing program. CSSS has been instrumental in the development of policy for the program.

CSSS totally revised all supply carts for the nursing units and implemented a more responsive delivery schedule. This has decreased the exchange cart inventory and has allowed us to reduce the size of the staff and increase the number of hours of operation on the weekends, and has provided overall better service.

CSSS replaced linen wrappers with non-woven disposable wrappers for sterile surgical packs. This has eliminated the frequent shortage of linen wrappers in the Clinical Center and has provided a relatively lint-free, hole-free wrapper.

## Training

Last year the American Society of Hospital Pharmacy's Residency Accreditation Committee urged the Clinical Center to increase the number of residents participating in the Pharmacy Department's residency program because of its unique nature. Following their recommendation, the Pharmacy Department increased the number of residents in their program from 2 to 5. In addition, the residency program was improved by preparing instructional objectives for

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each area of pharmacy practice.

The Pharmacy Service developed a program of formal quarterly conferences (Progress Review Conferences) to be held between each Pharmacy Service employee and his or her supervisor. The discussion covers performance and is meant to be a dialogue between supervisor and employee concerning the employee's progress in his or her job.

Pharmacy Service was involved in two training programs with the two area Schools of Pharmacy, the University of Maryland and Howard University. Two undergraduate students from the University of Maryland School of Pharmacy were trained in a structured externship program (Professional Experience Program) for two consecutive months. The program is designed to give the students practical experience in the practice of hospital pharmacy. One undergraduate student was accepted from the Howard University School of Pharmacy's Government Work-Study Program. The student spent 1040 hours in the Pharmacy Service in training. The training was divided into a distributive pharmacy rotation in Unit Dose Dispensing, in Intravenous Admixture preparation, and a clinical pharmacy rotation on the NCI nursing units.

Throughout the year pharmacists assigned to Pharmacy Service presented a variety of formal inservice education programs to the medical, nursing, and Pharmacy Department staffs. The titles include: "Incompatibilities of Intravenous Admixtures", "Management of Pain", "Anti-inflammatory Non-Steroidal Drugs", "Five Essential Drugs Used in Cardiac Arrest", "Use of Dobutamine", Use of Metoprolol", "Use of Disopyramide", "Use of Valproic Acid", "Use of Phenytoin", and "Food and Drug Interactions".

A formalized orientation program for new pharmacists assigned to Pharmacy Service was developed. The program which includes slides and reading material, was designed in a competency based objective format. Five new staff pharmacists were trained in this program.

A continuing education and training program for Pharmacy Service technicians was developed and implemented. The objectives of the program were twofold: (1) to provide current information on new procedures and calculations pertinent to the technician's role, and (2) to provide information such as basic pharmacology of drug classes, selection of OTC drugs, etc., so that the technicians would have a better perception of general pharmacy practice.

A second undergraduate student in Howard University's Government Work-Study Program spent 900 hours training in the Pharmaceutical Development Service.

Two undergraduate students from Purdue University spent three months training in the Pharmaceutical Development Service as part of the Public Health Service Commissioned Officer Student Training and Externship Program (COSTEP).

The entire pharmacy staff from PDS took a 16-week pharmacokinetics course, taught by Dr. Joseph Adir from the University of Maryland, to increase their knowledge of clinical pharmacokinetics and the clinical use of investigational drugs.

In compliance with JCAH standards, CSSS instituted a monthly, documented inservice training and education program on infection control, sterilization and processing techniques, quality control, and product utilization. The success of the program can be measured by the increasing participation and enthusiasm of the employees. Moreover, the knowledge that the employees have gained has allowed greater flexibility in work assignments.

Development

Pharmacy Service developed a training manual for the Pharmacy portion of the MIS computer system. The manual covers both the pharmacist and pharmacy technician's capabilities on the MIS system and is in a self-teaching format.

A model quality assurance program was developed for all distributive services within the Pharmacy Service including unit dose dispensing, outpatient dispensing, and intravenous admixture preparation. The program is a formal procedure with criteria and standards for all aspects of pharmaceutical services to assure their quality. The program will be implemented throughout FY 80.

A new position of Clinical Pharmacy Coordinator was developed for the Pharmacy Service. The coordinator, under the direction of the Chief, Pharmacy Service, develops and implements all clinical pharmacy services including the clinical phase of the residency program, staff development, drug information services, programs for drug monitoring, patient counseling and other unit activities.

A program to evaluate and to measure outpatient distributive services was developed by a pharmacy resident. Each element of the prescription filling process was timed and these time elements were applied against the statistics in the outpatient monthly workload report to determine man-hours expended in prescription filling.

A somewhat similar method was developed to evaluate the filling of the unit dose carts by pharmacy technicians.

The IV emulsion of ethiodized oil which was formulated and developed for IV hepatography by the PDS has now been tested in ten patients. Preliminary results indicate that the emulsion is safe for human use at the present dose. Further studies will be carried out at higher doses.

Policies and Procedures Manual for the Pharmaceutical Development Service was updated to include improved procedures and also expanded to be more comprehensive.

Twenty-eight objectives were drafted for the PDS portion of the Pharmacy Residency Program. The residents will be expected to meet these objectives after they complete their four-week rotation through the PDS.

CSSS developed major lines of accountability for operations at the first line supervisor level. With the acquisition of the Assistant Chief, CSSS was able to develop the first line supervisors to a level where they are more directly accountable for the performance of their employees. This has resulted in responsiveness to the needs of the Service, as well as the improved performance and satisfaction of the employees.

Policies and procedures for the procurement responsibilities of the Pharmacy Department were revised and updated to reflect recent changes in controls applying to requisitioning and issuing of drugs and all other departmental procurement activities.

### Research

The stability of Vitamin $K_1$ in hyperalimentation fluids was studied by PDS using high pressure liquid chromatography (HPLC). It was concluded that if protected from light, a solution of 1 mg Vitamin $K_1$ in one liter of hyperalimentation fluid degrades less than 10% in 24 hours.

Because of the increased interest in freezing reconstituted solutions of pharmaceuticals for long-term storage and the lack of comprehensive theoretical information on their stability in frozen systems, a research project on these questions has been initiated by PDS. It is hoped that general guidelines for predicting the stability of drugs in frozen solutions will result from this research.

A study is being conducted by the PDS using HPLC to identify the degradation products in the presence of varied sugar, pH, and buffer concentration and to provide general guidelines for stability of penicillins in dextrose containing infusion fluids.

The PDS has developed an HPLC method to separate various thermal and photodegradation products of cisplatin in aqueous solution. The method will be used to substantiate some earlier kinetic and stability studies and also to identify the degradation products. A more detailed study of the effect of light on cisplatin stability has also been undertaken because of the need for this practical information.

A method to improve the stability of 5-Azacytidine in aqueous solution was studied by PDS. This involved the formation of a prodrug (with sodium bisulfite) which might be used to prepare a stable parenteral or oral dosage form of 5-Azacytidine. The efficacy of the prodrug will be evaluated in *in vivo* systems.

## IV. FUTURE OBJECTIVES

Pharmacy Service will develop a comprehensive program of clinical pharmacy services. The program will include: criteria-based drug monitoring on selected nursing units, overall drug utilization review program for selected drugs, and expanded drug information service. Guidelines for these programs will also be developed to include function, responsibility, and evaluation.

The use of MIS computer will be developed to provide the pharmacy with clinical information such as: flagging of potential drug-drug interactions; generating a drug information sheet for the patient to be used in counseling;

and a specific medication profile for each outpatient seen in the clinics/ Ambulatory Care Research Facility (ACRF).

The Pharmacy Service will implement formal quality assurance programs for all distributive and clinical services it provides.

The PDS plans to expand its clinical pharmacokinetics service by developing assay methods for determining and monitoring plasma and CSF levels of investigational drugs and other research drugs.

The PDS plans to hire a research pharmacist to support the services of the clinical pharmacokinetics program.

The PDS will conduct compatibility studies on all drug combinations in the same I.V. infusion bottle prepared in the IVAU whose stability or compatibility is questionable and has not been reported in the literature.

CSSS plans to assume responsibility for the sterilization of all processed items used in the Clinical Center.

CSSS plans to develop a surgical case cart system for implementation in the ACRF. In this system, all of the instruments and supplies necessary for a surgical case will be prepared in CSSS and dispatched to the operating room. When the case is completed, the cart containing the used supplies and instruments will be returned to CSSS for disassembly and cleaning.

The Office of the Chief will begin developing an on-line computerized drug inventory control system. The purpose of the system is to improve purchasing practices and provide additional drug distribution control within the hospital. This system could include cost accounting by Institute, drug stock ordering from suppliers, and specialized management reports such as stock turnover reports, expired stock listings, optimum inventory levels, and drug usage trend forecasting. The system is intended to totally replace the existing hand maintained perpetual inventory card system, thereby eliminating all manual posting transactions.

## Table I
## Pharmacy Department Statistical Data

| | 1975 (Fiscal) | 1976 (Fiscal) | 1977 (Fiscal) | 1978 (Fiscal) | Est. 1979 (Fiscal) |
|---|---|---|---|---|---|
| PHARMACY SERVICE | | | | | |
| Outpatient prescriptions | 65,998 | 72,134 | 79,725 | 83,451 | 77,945 |
| Inpatient prescriptions | 2,593 | 1,559 | 1,297 | 436 | 266 |
| I.V. additives (bottles) | 89,411 | 112,845 | 140,930 | 163,978 | 151,158 |
| Drug vials reconstituted by I.V. Additive Unit | 39,015 | 43,320 | 42,520 | 41,312 | 30,519 |
| Sterile compounded items | 4,806 | 5,247 | 6,453 | 5,711 | 3,918 |
| Unit doses dispensed | 83,474 | 254,103 | 561,273 | 594,753 | 723,108 |
| Prepackaged items | 72,635 | 365,723 | 638,862 | 573,207 | 587,136 |
| Other items (mail-outs, bulk-compounding items, narcotics, requisitions, issues to I.V. area) | 274,691 | 282,727 | 298,061 | 258,335 | 173,302 |
| PHARMACEUTICAL DEVELOPMENT SERVICE | | | | | |
| Units developed and issued | 431,972 | 567,911 | 870,647 | 750,740 | 937,858 |
| Requests processed | 1,199 | 869 | 1,043 | 1,132 | 1,152 |
| Investigational drugs registered | 637 | 527 | 596 | 613 | 772 |
| New investigational drugs processed | 126 | 92 | 136 | 125 | 114 |
| PHARMACY OFFICER OF THE DAY | | | | | |
| Number of requests for service | 10,838 | 13,254 | 17,376 | 13,523 | 11,017 |
| MAIL-OUT PRESCRIPTIONS | | | | | |
| Number of prescription packages mailed | 1,478 | 1,527 | 1,558 | 2,048 | 1,911 |
| CENTRAL STERILE SUPPLY SERVICE | | | | | |
| Requisitions filled | 18,773 | 24,122 | 29,769 | 29,898 | 29,996 |
| Items issued | 904,848 | *2,524,596 | 4,893,103 | 7,297,564 | 9,732,170 |
| Trays and sets prepared | 15,193 | 13,068 | 14,213 | 15,506 | 11,983 |

*Due to change in method of tabulating items issued, statistical comparison between FY 1976 and previous years is impossible.

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Greene, R., Chatterji, D.C., Hiranaka, P.H., and Gallelli, J.F.: Stability of cisplatin in aqueous solutions. Am. J. Hosp. Pharm. 36: 38-43, 1979.

Vermess, M., Chatterji, D.C., Doppman, J.L., Grimes, G., and Adamson, R.H.: Development and experimental evaluation of a new contrast medium for computed tomographic examination of liver and spleen. J. Comput. Assist. Tomogr. 3: 25-31, 1979.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF<br>INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 05005-02 PHAR |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Development of Contrast Material for CT Scanning of Liver and Spleen

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| Michel Vermess | Assistant Chief | Diagnostic Radiology |
| Dulal C. Chatterji | Research Chemist | Pharmacy, CC |
| John Doppmann | Chief | Diagnostic Radiology |
| Richard Adamson | Chief | Laboratory of Chemical Pharmacology, NCI |
| George Grimes | Staff Pharmacist | Pharmacy, CC |

COOPERATING UNITS (if any)
Diagnostic Radiology, Clinical Center

LAB/BRANCH
Pharmaceutical Development Service; and Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.5 | None |

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER
☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

An emulsion of ethiodized oil was tested in normal and carcinogen induced hepatoma bearing monkeys. At a dose of 0.2 mg/Kg (one tenth the previously used dose) there was an average increase of 23 EMI units in the opacity of the liver. Opacification of spleen was even better. The visualization of tumors and small lesions in the monkey with hepatoma was significantly improved. Clinical trials have been initiated and the results are being presently evaluated.

Serial No. Z01 CL 05005-02 PHAR
Pharmacy Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
Oct. 1, 1978 - Sept. 30, 1979

Project Title: Development of Contrast Material for CT Scanning of Liver and Spleen

Previous Project Number: Z01 CL 05005-01 PHAR

Principal Investigator: Michel Vermess, M.D., Diagnostic Radiology

Other: Dulal C. Chatterji, Ph.D., Pharmacy Department
John Doppmann, M.D., Diagnostic Radiology
Richard Adamson, Ph.D., Laboratory of Chemical Pharmacology, NCI
George Grimes, B.S., Pharmacy Department

Cooperating Unit: Diagnostic Radiology Department, Clinical Center

Man Years: Total: 0.5
Professional: 0.5
Other: None

## Project Description

### Objective:

To evaluate various intravenous ethiodol emulsions for opacification of liver and spleen and in the diagnosis of hepatomas in monkeys.

### Methods Employed:

A Virtis homogenizer was used to make the emulsions and the size distribution of oil globules were evaluated by microscopy and Coulter counter. Conventional X-rays and CT scans were used for *in vivo* evaluation.

### Major Findings:

At an intravenous dose of 0.2 ml/Kg, emulsion E013 (which was found most satisfactory) increased the opacification of the liver by 23 EMI units. The opacification of the spleen was even higher. When injected to rhesus monkeys with carcinogen induced hepatomas, there was a significant improvement in the visualization of the tumors and small lesions.

### Significance to the Biomedical Research:

Visibility of the liver tumors in animals were significantly improved at a dose of 0.2 ml/Kg (one tenth of the previously used dose). If similar

REHAB. MED.
SOCIAL WORK
SPIRIT. MIN.

results are obtained in human subjects, this would be an important contribution to the diagnosis of liver cancers.

Proposed Course:

The contrast material will be clinically evaluated. Initially 10 patients will receive one dose of 0.2 ml/Kg of the contrast material with plans to increase the dose further if deemed safe and effective.

Honors and Awards:

None

Publications:

Vermess et. al.: Development and experimental evaluation of a contrast medium for computer tomographic examination of the liver and spleen. J. Computer Assisted Tomography 3: 25-31, 1979.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 05008-01 PHAR |

PERIOD COVERED
October 1, 1978 - September 30, 1979

TITLE OF PROJECT (80 characters or less)
Stability of Cisplatin in Aqueous Solutions

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| Raymond F. Greene | Staff Pharmacist | Pharmacy, CC |
| Dulal C. Chatterji | Research Chemist | Pharmacy, CC |
| Paul K. Hiranaka | Assistant Chief, Pharmaceutical Development Service | Pharmacy, CC |
| Joseph F. Gallelli | Chief, Pharmacy Dept. | Pharmacy, CC |

COOPERATING UNITS (if any)
None

LAB/BRANCH
Pharmaceutical Development Service

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.5 | None |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Cisplatin, in aqueous solution hydrolyses to give free chloride ion and the corresponding monohydroxy compound. The extent of decomposition is least in the presence of high chloride ion concentrations. Normal saline was judged to be the best vehicle of cisplatin infusion. Light increases the degradation of cisplatin and HPLC method showed additional degradation in products to the ones observed in dark. Therefore cisplatin solutions should be stored in dark.

PHS-6040
(Rev. 10-76)

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Serial No. Z01 CL 05008-01 PHAR
Pharmacy Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
Oct. 1, 1978 - Sept. 30, 1979

Project Title: Stability of Cisplatin in Aqueous Solutions

Previous Project Number: None

Principal Investigator: Raymond F. Greene, M.S.

Other: Dulal C. Chatterji, Ph.D., Pharmacy Department
Paul K. Hiranaka, B.S., Pharmacy Department
Joseph F. Gallelli, Ph.D., Pharmacy Department

Cooperating Unit: None

Man Years: Total: 0.5
Professional: 0.5
Other: None

## Project Description

### Objective:

To study the stability of cisplatin in infusion solutions and determine the vehicle in which it is most stable.

### Method Employed:

UV spectrophotometry and chloride ion titration were used to follow the rate and extent of degradation. The effects of pH, chloride ion concentration, drug concentration and extent of light exposure were studied.

### Major Findings:

Cisplatin, in aqueous solutions, hydrolyses to the corresponding hydroxy derivative. The reaction is reversible and hydrolyzed cisplatin is formed to the intact drug in the presence of a high chloride ion concentration. Normal Saline was found to be the best vehicle for storage of cisplatin infusion. Cisplatin should also be protected from light.

### Significance in the Biomedical Research:

The research led to the optimum condition for storage of cisplatin solutions. This not only assures accurate amount of drug being administered, but also minimizes the administration of degradation products which have unknown pharmacologic and toxic effects.

Proposed Course:

Using a HPLC method developed in our laboratory, we are planning to substantiate these kinetic results, identify the hydrolyzed degradation products, and conduct a more detailed study of the photodegradation of cisplatin.

Honors and Awards:

None

Publications:

Greene et. al.: Stability of cisplatin in aqueous solutions. Am. J. Hosp. Pharm. 36: 38-43, 1979.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 05009-01 PHAR |

PERIOD COVERED

October 1, 1978 to September 30, 1979

TITLE OF PROJECT (80 characters or less)

Stabilization of 5-Azacytidine in Aqueous Solutions

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| Dulal C. Chatterji | Research Chemist | Pharmacy, CC |
| J. F. Gallelli | Chief, Pharmacy Dept. | Pharmacy, CC |

COOPERATING UNITS (if any)

None

LAB/BRANCH

Pharmaceutical Development Service

SECTION

INSTITUTE AND LOCATION

CC, NIH, Bethesda

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.4 | 0.1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

In aqueous solutions maintained at pH 2.5, 5-Azacytidine (5-AC) forms a prodrug with sodium bisulfite. The prodrug is approximately 10 times more stable at pH 2.5 than 5-AC. The prodrug reverts back to 5-AC at physiological pH's. The prodrug has potential for a stable parenteral dosage form or an oral dosage form of 5-AC.

Serial No. Z01 CL 05009-01 PHAR
Pharmacy Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
Oct. 1, 1978 - Sept. 30, 1979

Project Title: Stabilization of 5-Azacytidine in Aqueous Solutions

Previous Project Number: None

Principal Investigator: Dulal C. Chatterji, Ph.D.

Other: Joseph F. Gallelli, Ph.D.

Cooperating Units: None

Man Years: Total: 0.5
Professional: 0.4
Other: 0.1

## Project Description

### Objective:

To improve the stability of 5-Azacytidine in aqueous solutions.

### Method Employed:

High Pressure Liquid Chromatography (HPLC) was used to analyze 5-Azacytidine in presence of degradation products. Spectrophotometry and HPLC was used to substantiate the proposed stabilization mechanisms. The effect of pH, buffer strength and amount of sodium bisulfite added were studied.

### Major Findings:

Stability of 5-Azacytidine in aqueous solutions was increased 10-fold by the addition of sodium bisulfite and maintenance of pH at approximately 2.5. Stabilization was attributed to the formation of bisulfite adduct across the reactive 5-6 double bond. The adduct was found to revert back to parent drug in physiological pH.

### Significance in Biomedical Research:

Increased stability of the 5-Azacytidine bisulfite prodrug should allow for easier infusion of drug solution over an extended period of time without the need to prepare a new infusion solution every 2-3 hours. The prodrug is formed only in acidic pH's, and remains stable in acidic pH in contrast to 5-AC alone which is unstable in acidic pH's. This makes the prodrug a likely candidate for the formulation and development of oral dosage form of the drug.

Proposed Course:

Evaluate the mixture of 5-AC and sodium bisulfite as a stable parenteral form and more importantly as an oral dosage form.

Honors and Awards:

None

Publications:

Chatterji, D.C. and Gallelli, J.F.: Stabilization of 5-Azacytidine by nucleophilic addition of sodium bisulfite. In Press. J. Pharm. Sci. 1979.

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SOCIAL WORK

SPIRIT. MIN.

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

REHABILITATION MEDICINE DEPARTMENT

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SOCIAL WORK

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October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## REHABILITATION MEDICINE DEPARTMENT

### I. Departmental Missions and Goals

The primary mission of the Rehabilitation Medicine Department is to provide the highest quality physiatric evaluation and treatment, physical therapy, occupational therapy, and speech therapy for Clinical Center patients referred by Institute physicians, and to develop indices to evaluate these services.

An equally important mission of the Department is to support efforts of and collaborate with Institute physicians engaged in research relevant to evaluation and treatment of patients with rehabilitation problems.

A third mission is to initiate both clinical and basic research independent of the Institutes in the rehabilitation of mentally and physically handicapped individuals.

A fourth mission is to advocate and defend the rights of handicapped persons, and to use education, preventive measures, and to support legislative efforts to accomplish this goal.

A fifth mission is to increase dialogue between NIH Rehabilitation Medicine Department and other academic and community facilities concerned with care of the handicapped.

### II. Departmental Activities

A. Staffing pattern is presented in Addendum I.
B. Patient Care Statistics

Patient care statistics are presented in detail in Tables 1-2 for Physical Therapy, 3-4 for Occupational Therapy, 5-6 for Speech Therapy, and Table 7 for Physiatrists.

### III. Major Progress

A. Patient Care and Professional Services

1. Occupational Therapy Service has continued to develop instruments for establishing reliable, reproducible methods for evaluating function and impact of therapy on disability.

    (a) Pre- and postoperative hand measurements are being obtained and translated into quantitative functional assessment.

(b) An educational program has been formalized and expanded whose goal is to present educational materials in a clear and relevant fashion to patients with arthritis. The content of this program is being readied for presentation to professional groups and for publication.

(c) A method to measure patients' understanding of rehabilitation treatment and principles in the management of arthritis was developed and used this year.

(d) The Occupational Therapy task-skills assessment form is being evaluated for inter-rater reliability. It is being expanded to include response to work therapy placement in order to further gauge functional performance.

2. Occupational Therapy has expanded its programs, providing more service in the following areas:

   (a) More work therapy placements have been secured and are supervised by a mental health occupational therapist

   (b) A program in NCI Pediatric Oncology has been formalized to assist in meeting the unique needs of this group in the following areas: (1) maintain coping skills during protracted hospitalizations which interrupt normal life patterns, (2) teach adaptation for independent function despite chronic illness, (3) assist in the establishment of contacts in the patient's home community in order to pursue rehabilitation goals following discharge from NIH

   (c) The use of new thermoplastic and soft materials in fabrication of upper extremity orthoses has been continued and expanded to improve patient care.

3. The Physical Therapy Service has continued to expand and improve patient care services in the following areas:

   (a) There is more complete care of the mastectomy patient from the immediate postoperative period when shoulder function is impaired to the later postoperative period when a wider range of breast prostheses are offered and when properly fitted

   (b) Management of pain using transcutaneous nerve stimulation is used frequently and is being done jointly with a local firm that supplies the patients with a rental unit and offers followup evaluation and reports back to the Rehabilitation Department.

4. The Rehabilitation Medicine Department has become increasingly aware of the need for discharge planning. Formal conferences for this purpose with Social Work and Nursing Departments have been initiated with NIAMDD.

5. Electrodiagnostic examination is being performed on selected patients referred to the Rehabilitation Medicine Department.

6. The Speech Pathology Service in conjunction with Diagnostic Radiology is providing ultrasound evaluation of articulation problems, and in patients with cleft palate and hearing deficiencies is adding biofeedback to ultrasound as a training technique.

B. Research

1. Occupational Therapy Service, Physical Disabilities Program, has provided quantitative functional evaluation of patients on a protocol for "Intravenous Cyclophosphamide in the Treatment of Rheumatoid Arthritis."

2. Summaries of advances in several areas of research are presented:

    (a) Twenty patients with primary or secondary Raynaud's phenomenon were taught either relaxation or temperature biofeedback. All patients learned the technique within 20 sessions. After training 19 patients were able to abort a classic Raynaud's attack. Change in digital temperature with exposure to 38°F approximated normal.

    (b) Twenty-seven patients receiving photochemotherapy for psoriasis were studied with respect to activity of arthritis. Two arthritic subgroups were distinguished: spondylitic and non-spondylitic. For the former, psoriasis was difficult to control, arthritis did not improve, and skin and joint activity varied independently. For the latter, skin clearance was easier to maintain, and arthritis control parallelled skin control.

    (c) Frequency of human lymphocyte antigens were determined in 58 patients with psoriasis, 48 with psoriatic arthritis, and 126 normal controls. HLA-A1, B13, B17 were increased in the psoriasis patients, HLA-A-26, B38 and DRw4 in the psoriatic arthritic population, and HLA-Cw6 and DRw7 increased in both groups.

    (d) Twenty-two patients with Ewing's sarcoma of the lower extremity who received 5000 rads and who were alive at least 2 years after diagnosis were evaluated for level of functional impairment. Thirteen had minor functional limitations, 6 had moderate limitation, 3 had severe limitation. Femoral fracture was a poor prognostic factor. One patient received amputation for complication of radiation therapy. Amputation is not warranted in the primary management of Ewing's sarcoma of the lower extremity, and functional impairment is usually minor.

(e) An investigation to evaluate and compare tongue movements in 30 normal and 30 neurologically impaired subjects using ultrasound with simultaneous audio and video tape recording during production of selected phonemes and words was begun. The performance of subjects with ALS, who have a motor deficit, will be compared to that of subjects with polymyositis who have myopathy. A comparison of the lingual and articulatory performance of these two types of diseases with normal speakers should provide a continuum of oral-motor function.

(f) A study is in progress to assess the "Energy Expenditure in Hemipelvectomy and Hip Disarticulation Amputees." This study is designed to assess:

(1) Comfortable speed of walking (C.S.W.)

(2) Energy expenditure and oxygen consumption of hip disarticulation and hemipelvectomy amputees during ambulation with or without prosthesis, and at rest. Other parameters such as respiratory ratio, etc., will be calculated. The same measurements will be made in age and sex-matched normal controls.

3. Publications

(a) A Prospective Study of the Rehabilitation of the Above-Knee Amputee with Rigid Dressings, W. Thorpe, L.H. Gerber, M. Lampert, J.K. Reed, I. Sabel, Clin. Orthop., in Press.

(b) Avascular Necrosis in Systemic Lupus Erythematosus: Silent Symmetrical Osteonecroses. J.H. Klippel, L.H. Gerber, L. Pollak, J.L. Decker, Am. J. Med., in Press.

(c) Chest Wall Syndrome: A Common Cause of Unexplained Cardiac Pain. S.E. Epstein, L.H. Gerber, J.S. Borer, JAMA, June 29, 1979, vol. 241, No. 26, pp 2793-2797.

(d) Photochemotherapy and Psoriatic Arthritis: A Prospective Study. S.G. Perlman, L.H. Gerber, R.M. Roberts, T.P. Nigra, W.F. Barth, An. Int. Med., in Press.

(e) Split Thickness Graft of the Plantar Surface of the Foot after Wide Excision of Cutaneous Neoplasm. E. Woltering, W. Thorpe, J. Reed, S. Rosenberg, J.Surg. Gynec, & Obstet., in Press.

### C. Training

1. The core curriculum for the Rehabilitation Medicine Department reflects its primary responsibilities in patient care. This has remained essentially unchanged from the previous year.

2. Weekly inservice training for the Department staff focused on state-of-the-art patient care techniques.

3. An intensive inservice training program has begun in biomechanics of the foot and ankle and in their podiatric management.

4. Staff members participated in specialty meetings including U.S. PHS Professional Association Annual Meeting, Physical Therapy Association Annual Meeting, Occupational Therapy Association Annual Meeting, Academy of Physical Medicine & Rehabilitation, Arthritis & Rheumatism Association, American Speech & Hearing Association.

5. Staff members have been invited to lecture on a variety of subjects including:

   (a) Biomechanics of Foot and Ankle Movement

   (b) "Semantic and Pragmatic Considerations in Language Therapy Programs for Language Disordered Children," Anne Arundel County Public Schools, Speech and Hearing Department, May, 1979

   (c) "Parkinson's Disease: Speech Therapy Techniques," American Speech & Hearing Association Prototype Workshop on Communication Problems and Behaviors of the Non-Institutionalized Elderly, February, 1979

   (d) Conservative Management of the Foot in Rheumatoid Arthritis

   (e) Rehabilitation of the Patient with Osteoarthritis.

## IV. Future Objectives

### A. Patient Care and Professional Services

1. The development of relevant and reliable evaluation tools for determining outcome following rehabilitation intervention is a primary objective. Through these evaluation indices, current practice can be assessed, and quality care can be assured.

2. The establishment of a multidisciplinary team or teams whose purpose will be to focus on total patient care needs and to participate in discharge planning is a top priority. These teams will include medical, nursing, social work and rehabilitation specialists.

3. Vigilance and participation in the renovation and construction of the Clinical Center in order to reduce architectural barriers and heighten awareness of the need for correction of these barriers.

4. Coordination of a program to meet some of the psychological and physical needs of patients in intensive care will be one of our goals for FY 1980.

5. The application of new technology in the use of thermoplastic agents in the construction of upper and lower extremity orthoses will continue to be developed in the coming years.

6. The application of information about energy expenditure and spinal mechanics in the lower extremity amputees to provide better ambulation training, prescription, and preventive care, is anticipated in the future.

7. The application of ultrasound to evaluation and treatment of oral-motor and swallowing problems is planned for the future.

B. Research

1. Continued development of evaluation indices and tools for all aspects of rehabilitation medicine will consume a considerable amount of time and effort in the Department.

2. A long-term diagnostic study of oral-motor performance in the elderly is being planned in conjunction with the Gerontology Research Center, NIA.

3. Use of language and evaluation of long and short term memory as a measure of higher cortical function in patients with SLE is being studied in conjunction with the Arthritis and Rheumatism Branch, NIAMDD.

4. An attempt to understand the neurophysiological basis for phantom pain and how to control it is a future objective for the Rehabilitation Medicine Department in conjunction with NCI Surgical Branch.

5. Emphasis will continue to be placed on diseases of the musculoskeletal system with study of biomechanics of motion.

6. The influence of the nervous system on musculoskeletal growth will be evaluated in patients with von Recklinghausen's neurofibromatosis with the Intramural Research Program, NINCDS.

C. Training

1. The core curriculum will be updated as new trends in Physical Medicine and Rehabilitation are appreciated.

2. An affiliation with George Washington University is being sought for placement of a 3rd year physical medicine and rehabilitation resident. This will provide academic affiliation for our Department and a good training opportunity for the resident.

D. Miscellaneous

1. Participation in DHEW-wide and NIH-wide committees for the handicapped will be a continued activity in coming years.

## Addendum I Rehabilitation Medicine Department Staffing Pattern

### Office of the Chief

| | |
|---|---|
| Chief, Rehabilitation Medicine Department | 1 |
| Assistant Chief | 1* |
| General Medical Officer | 1 |
| Secretaries | 3 (includes 1 part-time) |
| | 6 |

### Physical Therapy Service

| | |
|---|---|
| Chief, Physical Therapy Service | 1 |
| Assistant Chief | 1 |
| Staff Physical Therapists | 5 |
| Physical Therapy Assistants | 2** |
| | 9 |

### Occupational Therapy Service

| | |
|---|---|
| Chief, Occupational Therapy Service | 1 |
| Staff Occupational Therapists | 7+ (includes 2 part-time) |
| | 8 |

### Speech Therapy Service

| | |
|---|---|
| Speech Pathologist | 1 (part-time) |

* resignation effective 8/1/79

** Thelma Armstrong, retirement effective 7/14/79

+ Judy Schreiber, resignation effective 6/29/79
Grant A. Schofield, EOD 7/16/79
Part-time mental health occupational therapist EOD 8/26/79

## PHYSICAL THERAPY SERVICE

Table 1: Statistical Report Fiscal Year 1979
October 1, 1978 to September 30, 1979

| Institute | Number of Patients Treated FY 79 | | Number of Patient Visits FY 79 | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| NCI | 709 | 396 | 3838 | 1754 |
| NEI | 5 | -- | 7 | -- |
| NHLBI | 106 | 23 | 693 | 447 |
| NIAID | 119 | 23 | 640 | 42 |
| NIAMDD | 295 | 174 | 2049 | 1260 |
| NICHD | 81 | 3 | 207 | -- |
| NIDR | 1 | -- | -- | -- |
| NIMH | 119 | 11 | 442 | 14 |
| NINCDS | 513 | 86 | 2697 | 531 |
| TOTAL | 1948 | 716 | 10,573 | 4048 |

## PHYSICAL THERAPY SERVICE

Table 2: Comparative Statistics
Fiscal Years 1975 - 1979

| Fiscal Year | Number of Patients Treated | | Number of Patient Visits | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| 1975 | 1694 | 586 | 12960 | 2071 |
| 1976 | 2085 | 796 | 9016 | 2155 |
| 1977* | 2615 | 966 | 11513 | 2621 |
| 1978 | 1726 | 631 | 9569 | 3160 |
| 1979 | 1948 | 716 | 10563 | 4048 |

* Figures for FY 1977 represent 15-month totals because transitional quarter is included.

## OCCUPATIONAL THERAPY SERVICE

Table 3: Summary Report by Institutes of Number of Patients Treated, Number of Treatment Hours*
Fiscal Year - 1979

| Institute | Number of Patients Treated | | Number of Patient Treatments | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| NCI | 141 | 66 | 687 | 202 |
| NEI | 4 | -- | 45 | -- |
| NHLBI | 6 | 6 | 57 | 8 |
| NIAID | 28 | 11 | 187 | 46 |
| NIAMDD | 127 | 173 | 547 | 707 |
| NICHD | 41 | 18 | 335 | 96 |
| NIDR | -- | -- | -- | -- |
| NIMH | 257 | 8 | 8260 | 44 |
| NINCDS | 289 | 97 | 1462 | 454 |
| TOTALS | 893 | 379 | 11,580 | 1,557 |

## OCCUPATIONAL THERAPY SERVICE

Table 4: Comparative Statistics
Fiscal Years 1975 - 1979

| Fiscal Year | Number of Patients Treated | | Number of Patient Visits | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| 1975 | 1,220 | 359 | 10,622 | 358 |
| 1976 | 1,411 | 235 | 12,052 | 599 |
| 1977* | 1,774 | 294 | 14,595 | 519 |
| 1978 | 1,326 | 153 | 13,704 | 609 |
| 1979** | 893 | 388 | 11,872 | 1,550 |

* Estimates for July-September, 1979

** Figures for FY 1977 represent 15-month totals because transitional quarter is included.

## SPEECH THERAPY SERVICE

## Table 5: COMPARATIVE STATISTICS

Fiscal Year 1979*

| Fiscal Year | Number of Patients Treated | | Number of Treatment Hours | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| 1977 | 228 | 143 | 456 | 286 |
| 1978 | 361 | 311 | 626 | 597 |
| 1979 | 338 | 350 | 652 | 690 |

*1979 July, August, and September 1979 estimated

SPEECH THERAPY SERVICE

Table 6: SUMMARY REPORT BY INSTITUTE OF NUMBER OF PATIENTS TREATED, NUMBER OF TREATMENT HOURS

Fiscal Year 1979*

| Institute | Number of Patients Treated | | Number of Treatment Hours | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| NCI | 25 | 66 | 46 | 132 |
| NHBLI | 8 | 24 | 18 | 48 |
| NIAID | 31 | 16 | 54 | 32 |
| NIAMDD | 4 | 26 | 8 | 56 |
| NICHD | 3 | 53 | 7 | 106 |
| NIDR | -- | 48 | -- | 96 |
| NIMH | 26 | -- | 52 | -- |
| NINCDS | 238 | 92 | 478 | 204 |
| NEI | 2 | 3 | 4 | 6 |
| COURTESY | 4 | 22 | -- | 44 |
| SUBTOTAL | 341 | 350 | 667 | 724 |
| TOTAL | 691 | | 1,391 | |

* July, August, and September 1979 estimated

## REHABILITATION DEPARTMENT - OFFICE OF THE CHIEF

### Table 7: NUMBER OF PATIENT EVALUATIONS BY PHYSIATRISTS, FISCAL YEARS 1975-1978

| Fiscal Year | Total |
|---|---|
| 1975 | 897 |
| 1976 | 848 |
| 1977 | 1,625 (15 mos) |
| 1978 | 2,750 (12 mos)* |
| 1979 | 2,779 |

* Additional physician added to staff 8/77.

SOCIAL WORK

SPITIT. MIN.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 06 0001-3 REHAB |
|---|---|---|

PERIOD COVERED
November, 1976, through June, 1979

TITLE OF PROJECT (80 characters or less)

Correlation of Activity of Psoriatic Arthropathy with Psoriasis in Patients Receiving PUVA (Psoralen Ultraviolet A Therapy)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

N. L. Gerber, M.D., Chief, Rehabilitation Department, CC
Werner Barth, M.D., Washington Hospital Center (off site)
John Decker, M.D., ARB, NIAMDD
A. Eric Jones, M.D., Nuclear Medicine, CC
T. Nigra, M.D., Washington Hospital Center
Susan Perlman, M.D., Washington Hospital Center

COOPERATING UNITS (if any)

Washington Hospital Center, Rheumatology & Dermatology Section
Nuclear Medicine

LAB/BRANCH
Arthritis & Rheumatism/Rehabilitation Department, CC

SECTION

INSTITUTE AND LOCATION
NIAMDD/CC NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1 | 2/3 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

PUVA Therapy is recognized as an effective mode in treating psoriasis. It has no known anti-rheumatic properties. Approximately 15% of patients with psoriasis have an associated arthritis. This study monitors arthritis activity in patients with psoriatic arthritis during the course of PUVA Therapy, and correlates it with skin response to PUVA. Data shows two subpopulations of patients with arthritis: those with peripheral joint and those with axial involvement. The former group demonstrates a positive correlation between skin responsiveness and joint responsiveness. The latter group do not. The latter group has sacroilliitis and appears refractory to most forms of anti-inflammatory medication.

Project No. Z01 CL 06 0001-3 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1977, through June, 1979

Project Title: Correlation of Activity of Psoriatic Arthropathy with Psoriasis in Patients Receiving PUVA (Psoralen Ultraviolet A Therapy)

Previous Serial Number: Z01 CL 06 0001-2 REHAB

Principal Investigator: N.L. Gerber, M.D.

Cooperating Units: Washington Hospital Center, Department of Dermatology and Rheumatology
Diagnostic Imaging Section, CC

Man Years: Total - 1
Professional - 2/3

## Project Description

### Objectives:

Patients with psoriasis and psoriatic arthritis receiving photochemotherapy according to the Oral Methoxsalen-Photochemotherapy Cooperative Clinical Protocol (PUVA) have been followed to determine the effect of PUVA on skin and joint disease, and to determine if a correlation exists between skin and joint activity.

### Materials and Methods:

All were treated with PUVA until skin clearing (95%) and were then placed on maintenance PUVA schedules. Assessment at regular intervals included % psoriatic skin, articular index of peripheral and root joints (AI), visual analog scale, baseline x-rays and serial joint scans.

Twenty-seven patients have been followed. They were later subdivided into 2 groups: 21 with asymmetric seronegative peripheral arthritis (P) and 6 with active peripheral joint disease meeting New York Criteria for ankylosing spondylitis (S). S and P subgroups have been followed for a mean of 69 and 29 weeks, respectively. P had a higher initial AI (63 vs 50), but S had greater % skin involved (52 vs 39), longer duration of psoriasis (22 vs 16 yrs). 6/6 and 18/21 P cleared skin on PUVA. In contrast, mean % improvement in AI after initial skin clearing was 16% for S vs 49% for P. After first skin clearing, there were 10 skin flares per 280 patient-weeks in S receiving maintenance PUVA vs 2 skin flares per 171 patient-weeks in P. For these two P patients, joint flares were temporally related to skin flares. S skin and joint activity appeared to vary independently.

## Significance to Biomedical Research:

This study suggests there are at least 2 clinical subgroups of patients with psoriatic arthritis and each responds differently to control of underlying skin disease. For P skin clearing is associated with significant improvement in arthritis. For patients with S, the course of skin and joint disease varies independently.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 06 0005-2 REHAB |

PERIOD COVERED
February, 1977, through June, 1979

TITLE OF PROJECT (80 characters or less)
Biofeedback in the Management of Raynaud's Phenomenon

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

N.L. Gerber, M.D., Chief, Rehabilitation Department, CC
Cynthia Smith, OTR, Occupational Therapy Service, CC
Tim Reyburn, OTR, Occupational Therapy Service, CC
Andy Novick, RPT, Physical Therapy Service, CC
Elaine Bardo, OTR, Occupational Therapy Service, CC

COOPERATING UNITS (if any)

LAB/BRANCH

SECTION
Rehabilitation Department

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

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|---|---|---|
| TOTAL MANYEARS:<br>3/5 | PROFESSIONAL:<br>1/5 | OTHER: |

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients with primary or secondary Raynaud's phenomenon were randomized to receive relaxation training or temperature biofeedback in an attempt to relieve symptoms of Raynaud's phenomenon and control the temperature of the distal digits. Patients were monitored for skin temperature during training sessions, and placed in a 38° F room with constant temperature monitoring. Post-training, patients were able to control temperature better and keep hands warmer in ambient outdoor temperature and in the cold room. Both groups of patients did equally well in terms of control of temperature and in areas of symptom control.

Project No. Z01 CL 06 0005-2 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1977 through June, 1979

Project Title: Biofeedback in the Management of Raynaud's Phenomenon

Previous Serial Number: Z01 CL 06 0005-1 REHAB

Principal Investigator: N.L. Gerber, M.D.

Others: Cynthia B. Smith, OTR, Occupational Therapy Service, CC
Tim Reyburn, OTR, Occupational Therapy Service, CC
Andy Novick, RPT, Physical Therapy Service, CC
Elaine Bardo, OTR, Occupational Therapy Service, CC

Man Years: Total -
Professional -

## Project Description

This study was designed to evaluate the efficacy of autogenic training in the management of Raynaud's phenomenon. Biofeedback has been demonstrated effective in control of cardiac arrhythmias, bowel incontinence and other autonomic functions. Its efficacy in management of Raynaud's remains unproven.

Because little is known about the kinetics of response of skin temperature to cold, a further objective is to evaluate the normals response to 38° F cold and compare it to the Raynaud's patient.

## Materials and Methods:

Twenty patients, with primary or secondary Raynaud's phenomenon, who demonstrated white/blue/red color change when placed at 38° F for 3 minutes, were selected for study. Each was randomly assigned to receive temperature biofeedback or relaxation techniques. All had 20 hours of training, kept accurate logs of their Raynaud's attacks, and were re-evaluated after training.

## Major Findings:

All patients completed training. In the laboratory, 19 patients raised their skin temperature consistently during final 5 training sessions with an average increase of 6° F. Average digital temperature of 74° F increased from pre-training level of 77° F (68° - 87°) to 84° F (77° - 92°) post-training; and at 38° F for 3 minutes increased from 66° F to 71° F.

Post-training, 19 did not develop the 3-color change after 3 minutes at 38° F. A significant change in kinetics of skin temperature at 38° F was noted. Prior to training, patients with Raynaud's phenomenon would drop 10° F within one minute of entering the 38° F cold room. Post-training, the temperature drop was 8°F over a three-minute period, thus approximating the normals' response to cold.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Zo1 CL 06 0006-1 REHAB |

PERIOD COVERED
October, 1978 to June, 1979

TITLE OF PROJECT (80 characters or less)

The Diagnostic Capabilities of Ultrasound in Conditions Causing Oral-Motor Dysfunction

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Barbara C. Sonies, M.A., Rehabilitation Department, CC
Thomas H. Shawker, M.D., Diagnostic Radiology, CC
Thomas E. Hall, M.S., DRS:BEI
Willard C. Whitehouse, B.S., OCRI:CC
Lynn H. Gerber, M.D., Rehab:CC
Stephen B. Leighton, ScD. R:BEI

COOPERATING UNITS (if any)

BEI, Diagnostic Radiology, T.V. Engineering

LAB/BRANCH

SECTION
Rehabilitation Department

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1/5 | 1/7 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It has been difficult to correlate clinical impressions of oral-motor dysfunction and tongue function without using invasive procedures. A real-time with ultrasonic imaging system using a B-scan mechanical sector with simultaneous audio and video signals was developed to evaluate the range of tongue motions used during speech articulation. Thirty normal subjects were studied to obtain normalized tongue configuration graphs and durational data on production of selected phonemes. Measures of amplitude and velocity of tongue motions on these phonemes is being determined. Preliminary results indicate that ultrasound provides a reliable pattern of tongue movement in normals. Patients with amyotrophic lateral sclerosis and polymyositis will be studied to establish a continuum of oral motor function to differentiate between normal and impaired speech mechanisms.

Project No. Z01 CL 06 0006-1 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through June, 1979

Project Title: The Diagnostic Capabilities of Ultrasound in Conditions Causing Oral-Motor Dysfunction

Principal Investigator: Barbara C. Sonies, M.A.

Others: Thomas H. Shawker, M.D.
Thomas E. Hall, M.S.
Willard C. Whitehouse
Lynn H. Gerber, M.D.
Stephen B. Leighton, ScD.

Cooperating Units: Biomedical Engineering & Instrumentation Branch
Diagnostic Radiology
T.V. Engineering

Man Years:
Total - 1/5
Professional - 1/7

## Project Description

### Objectives:

1) To compare and evaluate tongue movement in normal and neurologically impaired subjects using ultrasonic imaging with simultaneous audio and video tape recording of phonemes selected to represent the range of tongue motion during articulation. The performance of patients with ALS, a neuromotor deficit, will be compared to that of patients with polymyositis who have myopathy; 2) To establish a continuum of oral-motor function for use in clinical examination; 3) To determine whether ultrasonic imaging of oral performance is sufficiently sensitive to detect progressive changes in oral-motor function.

### Materials and Methods:

Thirty normal subjects ages 25 to 65 who did not have obvious speech or dental impairment were evaluated using ultrasonic imaging of tongue motion during the production of 5 phonemes spoken singly and in various combinations. Subjects were seated in an appropriately designed wheelchair with a headrest and mirrors. A specially constructed ultrasonic transducer was positioned manually behind the mental symphysis of the mandible in the median sagittal plane. Simultaneous front and side views of the subject's face were monitored through the mirrors mounted on the chair. All stimuli and responses were recorded on videotape for later analysis. Signals were recorded both visually and auditorially. Normalized tongue configuration graphs are being derived for each phoneme using a stop-frame analysis of each phoneme. The amplitude and velocity of the tongue during production of phonemes is being obtained. We plan to evaluate 15 patients.

Major Progress:

A non-invasive, reliable method for studying oral-motor functions using a real-time ultrasonic imaging system has been developed cooperatively with diagnostic radiology, biomedical and television engineering. This unique system produces simultaneous auditory and visual signals which correlate with tongue motions during speech production. Thirty normal subjects have been evaluated to determine a baseline of lingual performance from which to compare patients with neurologic and motor dysfunction. It appears that this system will have significant diagnostic capacities.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 06 0007-1 REHAB |

PERIOD COVERED
February, 1979 through July, 1979

TITLE OF PROJECT (80 characters or less)

Oxygen Consumption and Energy Expenditure in Hemipelvectomy and Hip Disarticulation Amputees

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Farhad Nowroozi, M.D.
Lynn H. Gerber, M.D.
Mario Salvanelli, RPT

COOPERATING UNITS (if any)

None

LAB/BRANCH

SECTION
Rehabilitation Department

INSTITUTE AND LOCATION
CC. NIH, Bethesda, Maryland 20205

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|---|---|---|
| TOTAL MANYEARS:<br>1/5 | PROFESSIONAL:<br>1/10 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This study is designed to assess: 1) comfortable speed of walking (C.S.W.), and 2) energy expenditure and oxygen consumption of high level lower extremity amputees (hip disarticulation and hemipelvectomy) during ambulation with or without prosthesis, and also at rest, breathing room air. Other parameters such as respiratory exchange ratio, etc., will also be calculated. These respiratory and metabolic measurements will be measured in a group of normal individuals age and sex matched.

SOCIAL WORK

SPITIT. MIN.

Project No. Z01 CL 06 0007-1 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
February, 1979 through July, 1979

Project Title: Oxygen Consumption and Energy Expenditure in Hemipelvectomy and Hip Disarticulation Amputees

Principal Investigator: Farhad Nowroozi, M.D.

Other Participants: Lynn H. Gerber, M.D.
Mario L. Salvanelli, RPT

Man Years: Total - 1/5
Professional - 1/10

## Project Description

### Objectives:

This study is designed to assess: 1) comfortable speed of walking (C.S.W.), and 2) energy expenditure and oxygen consumption of high level lower extremity amputees (hip disarticulation and hemipelvectomy) during ambulation with or without prosthesis and also at rest, breathing room air. Other parameters such as respiratory exchange ratio, etc., will also be calculated. These respiratory and metabolic measurements will be measured in a group of normal individuals age and sex matched.

### Materials and methods:

C.S.W. in high level of amputation will be measured by asking the patient to walk 4 x 100 m at their comfortable speed while breathing through mouthpiece with nose clip on. Metabolic and respiratory parameters will be measured after a 15 min. rest, walking at C.S.W., fastest speed of walking (F.S.W.), slowest speed of walking (S.S.W.) while wearing the prosthesis and breathing through mouthpiece. These parameters will also be measured while the patients are walking without prosthesis, but with 2 crutches. Post exercise measurements will be then carried out.

Major finding:

None. Study in process at the present time; insufficient data to report.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 06 0008-1 REHAB |

PERIOD COVERED

January 1, 1979, through January, 1980

TITLE OF PROJECT (80 characters or less)

A Randomized Prospective Study of the Effect of Early versus Delayed Physical Therapy in the Patient Undergoing Axillary Dissection

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Steven A. Rosenberg, M.D., Surgery Branch, DCT, NCI
Michael Lotze, M.D., Surgery Branch, CT, NCI
Lynn H. Gerber, M.D., Rehabilitation Medicine, CC
Mary Duncan, RPT, Rehabilitation Medicine, CC
Farhad Nowroozi, M.D., Rehabilitation Medicine, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH

SECTION

Rehabilitation Department

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

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|---|---|---|
| TOTAL MANYEARS: 1 1/2 | PROFESSIONAL: 1 1/2 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients with melanoma or breast carcinoma undergoing axillary dissection are randomized to receive early or delayed shoulder mobilization following surgery. The study is designed to answer two questions: does Physical Therapy immediately post-op. interfere with wound healing; does Physical Therapy immediately post-op offer more effective treatment for shoulder function in this population. Eighteen patients have been entered into the study, but data is not yet definitive.

Project No. Z01 CL 06 0008-1 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
January, 1979, through January, 1980

Project Title: A Randomized Prospective Study of the Effect of Early versus Delayed Physical Therapy in the Patient Undergoing Axillary Dissection

Principal Investigator: Steven A. Rosenberg, M.D.

Other Participants:
Michael Lotze, M.D.
Lynn H. Gerber, M.D.
Mary Duncan, RPT
Farhad Nowroozi, M.D.

Man Years: Total - 1 1/2
Professional - 1 1/2

## Project Description

### Objectives:

This protocol is designed to answer two basic questions: (1) Does physical therapy immediately postoperatively interfere with wound healing? (2) Is immediate postoperative physical therapy more effective in rehabilitating the axillary dissection patient than a program that is less vigorous and delayed until wound healing is more progressed?

### Materials and methods:

All patients about to undergo axillary dissection for either melanoma of the upper extremity or upper torso and those patients about to undergo modified radical mastectomy with lymph node dissection will be eligible for this study. Patients who have preexisting conditions that would affect their neck or shoulder function are not eligible for the protocol.

Following initial outpatient evaluation and assessment of suitability for inclusion in the axillary dissection protocol, patients who agree to enter this study will be randomized into either vigorous or conservative physical therapy groups.

Stratification will be done for: (1) Age - greater or less than 50 years, (2) Tumor type, primary melanoma versus breast carcinoma.

**Major findings:** Inadequate data.

### Significance to Biomedical Research:

This study will help answer the questions of how best to rehabilitate patients undergoing axillary dissection.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 06 0009 -1 REHAB |

PERIOD COVERED
June, 1978, through June, 1981

TITLE OF PROJECT (80 characters or less)

Intravenous Cyclophosphamide in the Treatment of Rheumatoid Arthritis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

John H. Klippel, M.D., ARB, NIAMDD
John L. Decker, M.D., ARB, NIAMDD
Jacob Karsh, M.D., ARB, NIAMDD
Paul Plotz, M.D., ARB, NIAMDD
Lynn H. Gerber, M.D., Rehabilitation Medicine, CC

COOPERATING UNITS (if any)

LAB/BRANCH
Arthritis & Rheumatism Branch/Rehabilitation Medicine, CC

SECTION

INSTITUTE AND LOCATION
NIAMDD/CC, NIH, Bethesda, Maryland 20205

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| **TOTAL MANYEARS:** 1/5 | PROFESSIONAL: 1/5 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The efficacy of intravenous cyclophosphamide in the treatment of rheumatoid arthritis is to be evaluated. Patients are randomly assigned cyclophosphamide or placebo, and are evaluated for disease activity using clinical, functional and serological assessments. To date only 6 patients have been entered into the study.

Project No. Z01 CL 06 0009 -1 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
June, 1978 through June, 1981

Project Title: Intravenous Cyclophosphamide in the Treatment of Rheumatoid Arthritis

Principal Investigator: John H. Klippel, M.D.

Other Participatients: John L. Decker, M.D.
Jacob Karsh, M.D.
Paul Plotz, M.D.
Lynn Gerber, M.D.

Man Years: Total - 1/5
Professional - 1/5

## Project Description

We propose to evaluate the therapeutic efficacy and toxicity of intravenous cyclophosphamide given at two-month intervals in the treatment of patients with rheumatoid arthritis.

### Materials and methods:

This study will be a double-blind trial of 4 infusions of either intravenous cyclophosphamide (1 gram per meter squared, or less) or saline to be given at two-month intervals for six consecutive months.

Patients will be assigned to a treatment group according to a randomized schedule allocating 10 patients with rheumatoid arthritis who satisfy the admission criteria into each of the two treatment groups.

For each patient entering the study, a study coordinator and study observer will be assigned from among the study investigators. The responsibilities of these persons for the entire duration of the study for that patient are as follows:

a) Study coordinator:
    1) determine and order each dose of medication
    2) record side effects observed during the study
b) Study observer:
    1) perform and record the results of all clinical asessments; these observations will be made without knowledge of hematologic studies or symptoms developing during the study.

Major findings: Inadequate data collected to date.

Significance to Biomedical Research:

This study attempts to determine toxicity and efficacy of periodically administered cyclophosphamide in patients with rheumatoid arthritis. Additional information may be obtained with respect to evaluation of patients and correlation of clinical, functional, and serological parameters.

SOCIAL WORK

SPITIT. MIN.

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

SOCIAL WORK DEPARTMENT

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SPITIT. MIN.

October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## SOCIAL WORK DEPARTMENT

### I. DEPARTMENT MISSIONS AND GOALS

The Social Work Department of the Clinical Center is responsible for providing comprehensive social services which are implemented through individual social casework, social group work, social agency liaison work, and cross-discipline teamwork. The goals of these methods are (1) to modify or resolve personal difficulties and environmental conditions which interfere with patient-family participation in biomedical research; (2) to promote patient-family capabilities for obtaining maximum benefit from hospital-based services; (3) to prevent patient-family psychosocial deterioration as a consequence of illness and disease; (4) to establish linkages for patient-family use of community and interagency entitlements; (5) to collaborate and plan with multidiscipline teams to develop services and activities which impact on the patients' understanding and expectations; (6) to develop and maintain training programs for social work students and to participate in programs for other health arena students; and (7) to develop social work research to examine methods and systems which are involved in delivery of social services in the health arena. In summary, the overall mission of the Social Work Department is to provide comprehensive social services to biomedical research patients and, simultaneously, to reinforce rapport between the investigative/therapeutic systems and the patient/family systems.

### II. DEPARTMENT ACTIVITIES

#### Staffing Patterns

The Department's professional positions were assigned as follows: Office of the Chief - 2 full-time; Cancer Social Work Section - 7 full-time and 1 part-time; Child Health and Human Development Social Work Section - 2 part-time; Heart, Lung, and Blood Social Work Section - 3 full-time and 2 part-time; Allergy and Infectious Diseases/Arthritis, Metabolism and Digestive Diseases Social Work Sections - 2 full-time and 2 part-time; Neurological and Communicative Disorders and Stroke/Eye Social Work Sections - 2 full-time. Seventeen social workers were full-time and five social workers were under a 40-hour work week staffing pattern. Four social work representatives were employed in the Department during the Summer 1979.

#### Administrative Components

The Department's major task was to prepare for a social work audit designed to meet patient care evaluation guidelines set by the Joint Commission on Accreditation of Hospitals, supported by the Clinical Center and promoted by relevant professional organizations; namely, the Society for Hospital Social Work Directors of the American Hospital Association and the National Association of Social Workers, Inc.

To apply staff development principles, four professional staff workshops were held weekly over a 4-week period and three small study-groups were held weekly over a 3-week period. Discussion and planning guidelines were taken from selected literature and experience-based audit process guidelines by major general hospital social work departments.

The selected audit topic was the social work assessment. After refinement of the audit criteria and process, the first review was scheduled for August 1979.

Examples of ongoing tasks for the Department include (1) further refinement of the social work audit process; (2) identification of problems in the audit process; (3) development and implementation of solutions; (4) evaluation of the social work record framework and Medical Information System (MIS) matrices; and (5) implementation of the peer review process. From accurate identification of social problems and stress (the application of the social work framework for social diagnosis, assessment, and treatment) a social problem and service classification system can be developed. Identification of social problems and the range of compexity of these problems for which clinical social workers provide treatment together contain fundamental information for enriching the Department's current statistical report and provide the foundation for preparing a data retrieval system.

The major objectives of the Performance Standards and Appraisal Committee were absorbed in the preparation for a social work audit. These objectives included: (1) developing criteria and methods for evaluating social work practice in the Clinical Center; (2) promoting professional growth by investment in formal and informal education opportunities; and (3) institutionalizing an evaluative attitude, departmentally and individually.

## Intramural Activities

The Social Work Department was well integrated into the Clinical Center's projects and committees. Social workers were appointed to serve on Committees which included NHLBI Clinical Research Sub-Panel, Clinical Center Quality Assurance Committee,the Pediatric Policy Committee, the Equal Employment Opportunity Committee, the Architectural Barrier Committee, the Awards Board, the Recreation and Welfare Committee, the National Eye Institute Protocol Review Committee, the Committee on Guidelines for Consent for Research Involving Children, NICHHD Clinical Review Sub-Panel, Federal Women's Program - NIH EEO, and Women's Advisory Committee - CC.

The six-member Nursing/Social Work Liaison Committee held its first meeting on April 18, 1979. Three nurses and three social workers serve on this Committee. Declared goals and purposes of the Committee include role interpretation, information exchange about structural changes, and joint work on projects of mutual interest. Management of adolescents within the

Clinical Center and improvement of liaison with NIMH for psychiatric consultation were two areas of concern given high priority for discussion. Other intramural activities included information, orientation, or planning contacts with the Nutrition Department, the Patient Activities Department, the Clinical Center Volunteers, the Nursing Department - MICU, and the Rehabilitation Department.

Two clinical social workers provided either periodic consultation on personnel problems or leadership to ongoing stress-oriented groups for nursing staff on 8-East, NHLBI, and on 9-East, NICHHD.

## III. MAJOR PROGRESS IN RESEARCH, SERVICES, TRAINING AND DEVELOPMENT

### Research

The Program Supervisor, Cancer Social Work Section, participated in a Study of the Impact of Ongoing Comprehensive Education and Orientation on Breast Cancer Patients. A new Acne Study on NCI Dermatology Service required this supervisor's involvement in study preparation and in screening and evaluation of such patients for admission to the study.

The clinical social worker assigned to Radiation Branch, NCI, developed plans for preadmission intervention of preventive nature for the new protocol esophogeal cancer patients. The goals of the early intervention plans included assistance to these patients for easing the transition from disadvantaged, low income geographic and cultural regions, into the domain of biomedical research.

Comparable preadmission social work intervention was effected in the Heart, Blood, and Lung Social Work Section on Cardiology and on Pulmonary/Hematology Services. NCI Medicine Branch and Surgery Branch social workers have utilized screening clinic for early intervention/prevention services. The social work screening clinic approach has been in place for a considerable length of time.

### Progress in Training

The Department has ongoing training affiliation with the School of Social Work and Community Planning, University of Maryland, Baltimore, Maryland; and the School of Social Work, Howard University, Washington, D. C. Two Howard University social work students received their master's degrees in May 1979, and in September 1979 two students entered field placement with the Department. Two Maryland University social work students completed their field experience in December 1978, and in January 1979 three students entered field placement with the Department. These three students will complete their field assignments in December 1979.

### Staff Education

Direct service clinical social workers enrolled in continued education programs which were sponsored by professional associations, schools of social work, psychiatric treatment settings, and local universities.

Subject matter for these programs included mental health, child development, stress, death, and social work student teaching.

Mainstreaming Department members into the social work audit processes, principles, and requirements was a priority staff development project during this reporting period.

From a survey of interests, the Staff Education Committee learned that their colleagues want the services of a family therapist for knowledge-building and treatment-consultation purposes. In follow-up the Committee considered writing a proposal for programming a family therapy seminar which would meet continued education requirements.

## Community Related Activities

During the first quarter of this reporting period the NINCDS clinical social worker searched the Code of Federal Legislations because an Amyotrophic Lateral Sclerosis patient was denied service-connected disability benefits by the Veterans Administration. Search of the Code of Federal Legislations revealed that Multiple Sclerosis is ruled service-connected up to seven years following Armed Services discharge whereas Amyotrophic Lateral Sclerosis is ruled service-connected up to one year post-discharge. The social worker reported these facts to the president and vice-president of the Amyotrophic Lateral Sclerosis Society of America (ALSSOA) for their evaluation.

Months later, this information was formulated for legislative change through close collaboration and consultation among the ALSSOA officials, the Chief, Neuromuscular Disease and the NINCDS social worker. Legislative action "began for coverage of progressive muscular atrophy;" the above team edited, then recommended, and achieved rewording, "coverage of ALS and its various forms." The long legislative process has begun.

Through interpretation of need and collaborative efforts on behalf of patients, the NINCDS social worker reported that the Washington, D. C., Muscular Dystrophy Association (MDA) hired a case-aide to coordinate their patient services. Comparatively, MDA took an innovative position on service delivery.

The NINCDS social worker, assigned to Parkinsonian patients, reported that the Parkinsonian Society of Greater Washington, D. C., made program gains during its second year. The Society evolved from the Parkinsonian Group which was planned and led by the social worker who has continued to serve as consultant to the Society.

Additionally and consistent with the record of past activities, clinical social workers continued professional affiliations and patient service linkages with such organizations as the American Cancer Society, the Montgomery County Chapter of the American Red Cross, Division of Vocational Rehabilitation, American Heart Association, and Association of Pediatric Oncology Social Workers which was founded by Clinical Center social workers and other hospital-based oncology social workers. The Heart Section

Supervisor participated in a Colloquium on Psychoanalysis and Social Work which was sponsored by the American Psychoanalytic Association.

## Patient Services

Since 1975 clinical social workers expanded social work coverage by using social work groups to meet needs of patients and families. Group discussions included coping with the consequences of illness, the nature of disease entities, the utilization of social and health resources, and the purposes and methods of the hospital.

The Cancer Social Work Section in FY 1979 reported the following established groups: Special Ambulatory Care Patients (SACP), 2-East Parents' Group, Surgery Branch Screening Clinic, Medicine Branch Screening Clinic, 9-West NICHHD Parents' Group, Surgery Branch Inpatients, and the Teen Group. In planning stages are the following: 2-East Young Adults, NCI Breast Cancer Outpatients, and Preadmission Group for New Esophageal Protocol Patients.

Breakdown for the Social Work Sections serving NHBLI, NIAID, NIAMDD, NINCDS, and NEI, showed the following established groups: Asthma Outpatient Group, Chronic Disease Inpatient Group, Lupus "Rap" Group, Sickle Cell Anemia Group, Sjogrens Group, and Rheumatoid Arthritis Group. Established in 1976, the Parkinson Group was chartered in October 1977 as the Parkinsonian Society of Greater Washington, D. C.

Each Social Work Section reported increased activity with outpatients and preadmission patients. Social workers provided tangible solutions for travel, housing, and local transportation problems which were presented by patients and their caretakers. Social workers alleviated psychosocial, cultural, language, and financial difficulties not only among local and nationwide preadmission and clinic patients, but also among the preadmission patient-citizens of foreign countries.

Among the rapid turnover in patient population, social workers reported an increase in demand for crisis-oriented interventions which were adapted to meet urgent needs of the "living alone" patient, to ameliorate behavioral difficulties of the distressed adolescents, to alleviate separation problems of the young parent and child, and to provide significant support for the families of patients in life-threatening crisis.

The two Social Work Sections reported lengths of stay to range from two days, two weeks, four months, to months. Hospital dependence, loss of role in the family, the workplace, and the community, loss of physical dependability and function, and changes in self-image, esteem and confidence were among other psychosocial, interpersonal and relationship problems which were identified and treated by clinical social workers. The individual casework approach was the social workers' method of choice for resolving the complex problems experienced by long-term patients and their families.

Social work intervention was in double demand in the cases of preadolescent and adolescent patients and their parents and siblings. Realization of the personal meaning and impact of chronic, progressive and often genetically-caused illnesses, in many cases contributed to disorganization in family systems, confounded parent-adolescent communication, disturbed sibling relationships, and depleted socioeconomic and interpersonal resources. For persons dealing with such complications, social workers sought to strengthen family coping methods, to reinforce through interdisciplinary teamwork the presenting family strengths, and to discover (or create) recreational, educational and social means for enhancing quality of life.

During FY 1979, social workers reported an increase in the numbers of patient care conferences which generaly were referred to as team conferences and multidiscipline conferences. Foremost, the team approach enhanced existing services and, at times, introduced new services to patients and their families. From team methods, the professionals gained not only job satisfaction rewards but also service delivery successes founded in the application of coordination, collaboration and communication technology.

Social workers were involved in liaison work with community agencies and in enabling work with heretofore self-sufficient families and persons. On personal levels, the utilization of tax and voluntarily supported health-social-financial maintenance systems can mean a loss of community-based self-esteem. Social workers helped patients and families resolve feelings which resulted from recognized dependence upon legislated and voluntary entitlements.

Table 1 shows a four-year breakdown of the delivery of social services to outpatients in preadmission, clinic, and follow-up status and to inpatients. In percentage terms, social service delivery to outpatients increased gradually while social service delivery to inpatients decreased proportionately. While staffing patterns remained fairly constant, expanding outpatient clinics, shortening periods of hospitalization and increasing rates of hospital admissions combined to produce time and caseload pressures upon the clinical social workers for maintaining rates of service delivery for inpatients and for increasing rates of service delivery for outpatients.

## Wig Contract

Consistent with past utilization of this service, approximately 327 wig requisitions (adult and child) were processed through the Social Work Department. Wig contracts were let in the amount of $28,000 during the past 12 months.

## Interment Allotments

Effective May 1977, th Social Work Department was assigned the decision-making responsibility for interment allotments. The chart, which follows, shows utilization frequencies of this resource.

UTILIZATION FREQUENCIES - INTERMENT ALLOTMENTS

| Fiscal Year | First Quarter | Second Quarter | Third Quarter | Fourth Quarter | TOTAL |
|---|---|---|---|---|---|
| 1978 | 12 | 12 | 9 | 7 | 40 |
| 1979 | 16 | 7 | 7 | - | 30 |

## On-Call System

Formalized in May 1977, the Department's on-call system was designed to provide social work coverage through week-day evenings, week-ends, and holidays. The following chart is a quarterly breakdown on the utilization of the on-call system.

UTILIZATION OF ON-CALL SYSTEM BY HOURS EFFECTIVE MAY 1, 1977

| Fiscal Year | First Quarter | Second Quarter | Third Quarter | Fourth Quarter | TOTAL |
|---|---|---|---|---|---|
| 1978 | 13hrs-33min | 25hrs-13min | 04hrs-15min | 11hrs-41min | 54hrs-42min |
| 1979 | 06hrs-15min | 08hrs-40min | 05hrs-05min | - | 20hrs-00min |

## NIH Patient Emergency Fund

Administered through the Social Work Sections and the Department, an array of services was available to Clinical Center patients and families. Patient Emergency Fund expenditures were for basic and miscellaneous necessities, local transportation for patients, room and board allowances for relatives, and special programs for patient attendance. The Fund has been kept viable by regular contributors and ingenious benefits. One source of income was the Annual Holidays of December gifts from NIH employees. A second source of income was the Annual Softball Game played this year between the NIH Gashouse Gang and the One and Only TV Nine team.

PATIENT EMERGENCY FUND BREAKDOWN

| | Deposits | Withdrawn | Average Exp. | Number of Patients Helped with PEF NCI | OTHER |
|---|---|---|---|---|---|
| July 1975-June 1976 | $37,000 | $47,900 | $172 | 169 | 109 |
| July 1976-June 1977 | $49,000 | $45,500 | $150 | 154 | 152 |
| July 1977-June 1978 | $53,000 | $62,300 | $216 | 145 | 144 |
| July 1978-June 1979 | $45,000 | $57,000 | $194 | 145 | 149 |

## IV. FUTURE OBJECTIVES

1. Maximized capacity for delivery of social services to Clinical Center patients who are in preadmission, clinic, and follow-up status.

2. Development of a retrieval mechanism to assemble aggregate data from the computer assisted social work record for the purposes of analyzing, evaluating, and improving social service delivery.

3. Development of methods for in-department patient care evaluations which meet accountability and quality control criteria as sanctioned by accreditation and standard-setting agents.

## TABLE 1

## FOUR-YEAR SUMMARY OF PATIENTS SERVED

| Patient Status | Patients Served<br>July 1975 – May 1976 |  | Patients Served<br>July 1976 – May 1977 |  | Patients Served<br>July 1977 – May 1978 |  | Patients Served<br>July 1978 – May 1979 |  |
|---|---|---|---|---|---|---|---|---|
|  | Number | % of Total | Number | % of Total | Number | % of Total | Number | % of Total |
| Preadmission | 144 | 2.0 | 109 | 1.4 | 91 | 1.0 | 186 | 2.3 |
| Clinic | 487 | 6.6 | 587 | 7.5 | 1,014 | 12.0 | 640 | 7.8 |
| Follow-Up | 1,548 | 19.9 | 1,593 | 20.4 | 1,422 | 17.0 | 1,668 | 20.2 |
| Outpatients Total | 2,179 | 28.5 | 2,289 | 29.3 | 2,527 | 30.0 | 2,494 | 30.3 |
| Inpatients Total | 5,240 | 71.5 | 5,513 | 70.7 | 5,941 | 70.0 | 5,742 | 69.7 |
| GRAND TOTAL | 7,419 | 100.0 | 7,802 | 100.0 | 8,468 | 100.0 | 8,236 | 100.00 |

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## TABLE 2
## INPATIENT COVERAGE BY PERCENTAGE

JULY 1977 through MAY 1978

| INST. | INPATIENT CENSUS | INPATIENTS SERVED | PERCENT COVERAGE |
|---|---|---|---|
| NCI | 3,426 | 2,099 | 61.3 |
| NHLBI | 1,850 | 1,396 | 75.5 |
| NIAID | 896 | 695 | 77.6 |
| NIAMDD | 883 | 673 | 76.2 |
| NINCDS<br>NEI | 1,214 | 713 | 58.7 |
| NICHHD | 340 | 365 | 93.2 |
| TOTAL | 8,609 | 5,941 | 69.0 |

JULY 1978 through MAY 1979

| INST. | INPATIENT CENSUS | INPATIENTS SERVED | PERCENT COVERAGE |
|---|---|---|---|
| NCI | 3,506 | 1,899 | 54.2 |
| NHLBI | 1,934 | 1,352 | 69.9 |
| NIAID | 873 | 695 | 79.6 |
| NIAMDD | 967 | 692 | 71.6 |
| NINCDS<br>NEI | 1,037 | 693 | 66.8 |
| NICHHD | 477 | 411 | 86.2 |
| TOTAL | 8,794 | 5,742 | 65.3 |

TABLE 3

Number of Clients Provided with Social Work Services

July 1978 through June 1979

| | PREADMISSION | | INPATIENT | | CLINIC | | FOLLOW-UP | | TOTAL PTS. | TOTAL FAMILY MEMBS. |
|---|---|---|---|---|---|---|---|---|---|---|
| | Pt. | Family Memb. | Pt. | Family Memb. | Pt. | Family Memb. | Pt. | Family Memb. | | |
| 1978 JULY | 6 | | 579 | | 73 | | 183 | | 841 | |
| | | 8 | | 376 | | 48 | | 80 | | 512 |
| AUG. | 11 | | 572 | | 70 | | 150 | | 803 | |
| | | 11 | | 380 | | 41 | | 55 | | 487 |
| SEP. | 10 | | 562 | | 65 | | 139 | | 776 | |
| | | 5 | | 359 | | 26 | | 58 | | 448 |
| OCT. | 25 | | 529 | | 39 | | 205 | | 798 | |
| | | 19 | | 375 | | 28 | | 62 | | 484 |
| NOV. | 34 | | 520 | | 50 | | 176 | | 780 | |
| | | 32 | | 338 | | 18 | | 75 | | 463 |
| DEC. | 16 | | 401 | | 45 | | 139 | | 601 | |
| | | 11 | | 277 | | 19 | | 46 | | 353 |
| 1979 JAN. | 8 | | 470 | | 76 | | 197 | | 751 | |
| | | 9 | | 361 | | 33 | | 70 | | 473 |
| FEB. | 19 | | 489 | | 40 | | 125 | | 673 | |
| | | 19 | | 262 | | 7 | | 49 | | 337 |
| MAR. | 9 | | 502 | | 36 | | 105 | | 652 | |
| | | 6 | | 328 | | 27 | | 36 | | 397 |
| APR. | 23 | | 535 | | 55 | | 112 | | 725 | |
| | | 20 | | 420 | | 32 | | 57 | | 529 |
| MAY | 25 | | 583 | | 91 | | 137 | | 836 | |
| | | 27 | | 379 | | 37 | | 51 | | 494 |
| JUNE | 37 | | 583 | | 57 | | 88 | | 765 | |
| | | 26 | | 404 | | 34 | | 30 | | 494 |
| | 223 | | 6,325 | | 697 | | 1,756 | | 9,001 | |
| | | 193 | | 4,259 | | 350 | | 669 | | 5,471 |

## TABLE 4
## GROUP ACTIVITY REPORT

*October 1978 through June 1979

| SECTION | RESEARCH ACTIVITIES | | PRACTICE-PROGRAM ACTIVITIES | | SWD ACTIVITIES | | COMMUNITY AND PROFESSIONAL ACTIVITIES | | TOTAL HOURS |
|---|---|---|---|---|---|---|---|---|---|
| | HOURS | % | HOURS | % | HOURS | % | HOURS | % | |
| NCI | 21 | 0.8 | 1,372 | 54.2 | 962 | 38.0 | 176 | 7.0 | 2,531 |
| NHLBI | 43 | 3.4 | 528 | 41.2 | 648 | 50.6 | 61 | 4.8 | 1,280 |
| NIAID | 1 | 0.1 | 298 | 72.0 | 109 | 26.4 | 6 | 1.5 | 414 |
| NIAMDD | 21 | 5.0 | 233 | 55.6 | 113 | 27.0 | 52 | 12.4 | 419 |
| NINCDS<br>NEI | 20 | 2.8 | 398 | 55.8 | 248 | 34.7 | 48 | 6.7 | 714 |
| NICHHD | 4 | 0.8 | 379 | 76.7 | 97 | 19.7 | 14 | 2.8 | 494 |
| TOTAL | 110 | 1.9 | 3,208 | 54.0 | 2,177 | 38.0 | 357 | 6.1 | 5,852 |

* Nine months of FY 1979

## TABLE 5
## NIH PATIENT EMERGENCY FUND EXPENDITURES

*October 1978 through June 1979

| MONTH | SPECIAL PROGRAM | PATIENT TRANSPORTATION | ALLOWANCE TO RELATIVES | PATIENT MISCELLANEOUS | BASIC NECESSITIES | TOTAL WITHDRAWN | TOTAL DEPOSITS |
|---|---|---|---|---|---|---|---|
| OCT. | 851.25 | 339.75 | 2,022.50 | 295.00 | 144.00 | 3,652.50 | 2,137.20 |
| NOV. | 643.50 | 183.30 | 3,344.00 | 254.25 | 237.00 | 4,662.05 | 5,079.63 |
| DEC. | 806.76 | 198.00 | 2,784.50 | 326.20 | 139.00 | 4,254.46 | |
| 1979 JAN. | 664.00 | 124.00 | 2,626.50 | 241.30 | 157.00 | 3,812.80 | 18,680.50 |
| FEB. | 598.00 | 106.00 | 2,214.00 | 264.60 | 188.00 | 3,370.60 | |
| MAR. | 855.25 | 96.00 | 2,758.60 | 275.00 | 285.67 | 4,270.52 | 5,999.99 |
| APRIL | 791.50 | 474.00 | 2,159.50 | 603.32 | 164.50 | 4,192.82 | |
| MAY | 616.50 | 239.55 | 4,111.00 | 451.00 | 200.50 | 5,618.55 | 2,428.46 |
| JUNE | 909.50 | 373.10 | 3,402.00 | 203.16 | 158.00 | 5,045.76 | 2,049.02 |
| TOTAL | 6,736.26 | 2,133.70 | 25,422.60 | 2,913.83 | 1,673.67 | 38,880.06 | 36,374.80 |

*Nine months of FY 1979

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October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

DEPARTMENT OF SPIRITUAL MINISTRY

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October 1, 1978 through September 30, 1979

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## DEPARTMENT OF SPIRITUAL MINISTRY

### OVERVIEW

The basic task of the Department was to provide spiritual ministry to patients and their families who welcomed the ministrations of a clergyman and to hold religious services in the hospital. It also included acting as liaison with religious groups not represented by the staff chaplains. Fundamental to this task was the bedside ministry to patients and family members and the religious services held in the fourteenth floor Chapel. Other tasks of the Department included consulting with fellow staff members of the Clinical Center, attending multidisciplinary conferences, membership on research committees, working with the N.I.H. EEO Council and EEO counseling, participating in education and orientation seminars, lecturing, and consulting with other clergy and community groups.

Statistics indicated the following average religious preferences of newly admitted patients: Jewish - 6%; Catholic - 26%; Protestant and others - 68%.

### STAFF

Chaplain LeRoy Kerney served as Chief of the Department and as a Protestant Chaplain. Chaplain Robert White and Chaplain William Payne were the other Protestant Chaplains.

Father Eugene Linehan, S.J. served in the hospital on a five day basis. Several part-time priests or pastoral associates assisted him in ministering to the patients and their families. They worked on days not covered by Father Linehan, brought Holy Communion to the bedside, made pastoral visits, and worked with many of the Spanish speaking families. A small group of seminarians from the School of Theology, Catholic University, came for supervised training during the school year.

Rabbi Joseph Levine served in the hospital on a half-time basis: Tuesdays, Thursdays and Friday afternoons. He also served in a similar capacity at St. Elizabeth Hospital, Washington, D. C. He was available for emergencies at the Clinical Center through the paging system.

## CHAPEL SCHEDULE

Regular chapel services were held during the year for the major faith groups. Mrs. Frances Viernstein was the Sunday Chapel organist  These services were:

Protestant: Sunday, 10:00 a.m. Holy Communion Service, the first Sunday of each month.

Catholic; Sunday and weekdays, 11:15 a.m. Daily distribution of Communion to bedridden patients.

Jewish: Friday, 4:30 p.m.

In addition to the regular services, these special services were held:

Protestant:
- World Wide Communion - 1st Sunday in October
- Thanksgiving Day Service
- Christmas Carol Service
- Christmas Day - bedside visitation
- Maunday Thursday
- Good Friday Service - (participation by Protestant and Catholic clergy and patients)

Catholic:
- Holy Days of Obligation Mass
- Special Blessing of Throats
- Distribution of Ashes - Ash Wednesday

Jewish:
- Rosh Hashana
- Yom Kippur
- Memorial Services
- Sukkot
- Chanukah
- Purim
- Passover
- Shavuoth

All three faiths extended the ministry of the Chapel services by broadcasting the services through bedside speakers for those unable to go to the Chapel and by visitation to bedridden patients. Appropriate sacraments were administered as requested.

## CHAPEL SERVICES

The daily 11:15 Catholic Mass provided a great resource for both patients and staff. As the Out-Patient Clinic develops, so does the attendance at this service and supplies spiritual nourishment and the sense of community sorely needed for so many of these patients who are filled with the anxiety of treatment.

One of the continuing highlights of ministry is the weekly Protestant worship in the Chapel where the people are constantly reminded in a dramatic way that they are not merely individuals facing difficult and trying situations, but that they are indeed part of the family of God and the communion of saints. Week in and week out, those who attend show a desire and the willingness to share in the worship service and, although often they begin as strangers, there develops a sense of unity and fellowship and mutual concern that makes worship at the Clinical Center a refreshing and strengthening experience.

The Friday afternoon Jewish service provided an opportunity for patients and whole families to examine feelings and behavior of fear and anxiety as well as participate in the more formal religious service. The Chanukah Service featured a chorus from the Jewish Community Center.

An Ecumenical Thanksgiving Service was held on Thanksgiving day. This is the second time such a service was held in the Clinical Center. Patients and their families were given an opportunity to share with each other through a drawing or words their thoughts on this particular holiday.

## PASTORAL MINISTRY TO PATIENTS AND THEIR FAMILIES

The Department attempted, when possible, to have a staff member visit all patients prior to major surgery, patients who were on the seriously ill list, and families of patients who died. All Catholic patients were contacted through the sacramental ministry of the Catholic chaplain. The Jewish chaplain was able to see all the patients of the Jewish faith. Most of the Protestant patients were visited. Priority was given to visiting the terminally ill, the seriously ill, patients scheduled for surgery, referrals by staff, relatives and pastors, as well as direct patient requests. Clergymen from the community were called upon to minister to special patients, e.g., patients requesting special rites from clergymen of their own denominations. These included several Greek Orthodox priests who were routinely called to minister to the Greek-speaking patients.

Pastoral problems which the chaplains encountered included: loneliness, grief, fear, guilt, anxiety, loss of spiritual meaning, boredom, identity crisis, changes in body-image and body-function. Pastoral methods included pastoral conversations, pastoral counseling, sacraments, blessings, prayer, scripture, and worship. On occasion, the chaplains helped patients and their families resolve dilemmas of conscience, conflicts of values, and difficulties in accepting radical therapies.

All members of the staff endeavored to be sensitive to the patient's own understanding of religion for himself, and, in turn, become a resource person for the patient to discover or rediscover his own spiritual strength.

The complex work of a chaplain called for familiarity with the medical situation, medical knowledge, sensitivity to emotional issues, and work with staff and family, and is illustrated by the following stories and reports.

A chaplain was asked by a fifteen year old girl to be baptized in her room. She was confined to bed and very seriously ill. The girl had a deep religious faith which enabled her to deal with her illness with much strength and courage. Her parents and younger sister were able to be present for the baptism. The sharing of this experience provided support and strength for both the patient and her family. The patient died two weeks after the baptism. The day before her death she shared with the chaplain how much comfort and hope the service of baptism had given her during that time.

A child's participation in Catholic life here demonstrated to the Catholic chaplain the value of such ministry. The child was here for one year and a half. Daily Sacramental life, especially rooted in the Eucharistic service, proclaimed the death of the Lord. This 14 year old child, victim of Ewing's sarcoma, was faithful at worship along with his mother and members of his family. As death approached, the request was made for the priest chaplain to come to his own home town to celebrate his funeral. When a fellow patient was dying next to his bed, eager staff was anxious to spare him the scene but he pulled back the shield-curtain and asked his mother: "Why do you grownups fear death; I'll be with him in a couple of weeks." The chaplain followed the child to celebrate his death, assuring family and friends that our concern here does not end with death.

A chaplain observed that contrary to what might be expected, it was the patients who came from the local community who often had the greatest difficulty in coping with their illnesses. The emotional strain of playing host and having to make daily reports to the next of kin often lead to a covert mutual hostility between patients and family that sometimes spilled over to hospital staff. Through his bedside pastoral counseling with patients, discussions with staff, informal conversations in the cafeteria, and frank dialogues at the weekly worship services when the whole family was present, channels of communication were established and maintained that helped the process of coping and healing.

Sometimes new technology results in unusual pastoral ministry. A woman who had returned a few months after successful open heart surgery with a minor complaint, turned out to have a terminal illness. She requested that her organs be donated and very little time was left to work out the arrangements. A large number of relatives were present and in disagreement about the patient's request. The chaplain and the doctor spent long hours helping the family understand the process involved. Because the patient had to be on a respirator many extra hours until a kidney transplant team was obtained, many disturbing questions were raised by family and staff to which the chaplain and the doctor responded. Even after the episode was over, help in sorting out feelings and ethical issues continued. Time was given to staff to ventilate their feelings and to grieve. The chaplain conducted the funeral and was able to bring back to the staff some feeling of completion and participation in the final events in the experience of the patient's family.

Pastoral Ministry Statistics For Two Typical Months:

| | | Protestant | Catholic | Jewish |
|---|---|---|---|---|
| Admissions | October 1978 | 427 (68%) | 162 (26%) | 34 (6%) |
| | May 1979 | 443 (66%) | 186 (27%) | 46 (7%) |
| Discharges | October 1978 | 648 (79%) | 141 (17%) | 34 (4%) |
| | May 1979 | 374 (66%) | 159 (28%) | 36 (6%) |

| | | Protestant | Catholic | Jewish |
|---|---|---|---|---|
| Pre-ops | October 1978 | 85 (69%) | 31 (25%) | 7 (6%) |
| | May 1979 | 48 (65%) | 18 (24%) | 8 (11%) |

## WORK WITH STAFF

Group seminars with staff members dealt with family, emotional, and treatment problems. Staff attended a number of weekly multidisciplinary meetings.

Frequent informal consultation with nurses, doctors, and social workers concerning a particular patient's progress and condition was helpful in carrying out an effective plan of pastoral care and visitation.

## RESEARCH COMMITTEES

Chaplain Kerney was a member of the National Institute of Mental Health Research Review Committee and of the National Institute of Neurological and Communicative Disorders and Stroke Research Review Committee. He also served on a Research Committee of the Department of Defense to review a special project.

## EEO

Chaplain White functioned as an EEO Counselor and as a member of the CC-EEO Advisory Council.

## EDUCATION AND TRAINING

Chaplain Kerney presented his slide-sound show, "A Time To Heal", to four groups of staff and student nurses.

Chaplain Kerney met with a group of nurses from the Medical Intensive Care Unit for an Orientation to the Department of Spiritual Ministry. A similar orientation session was held for a group of persons from Patient Activities.

Father Linehan participated in an education program for Cancer Work Study students.

## CONSULTATION

Chaplain Kerney served on a review committee for students enrolled in a program of Clinical Pastoral Education at Walter Reed Medical Center, Washington, D.C.

## COMMUNITY EDUCATION

Chaplain Kerney lectured at the Ohio Chaplains' Association, Columbus, Ohio.

Chaplain Kerney was one of two speakers who gave the Davidson Lecture on "The Physician and Clergyman as Patients", sponsored by the Medical Society of the District of Columbia, Washington, D.C.

Chaplain Kerney was the banquet speaker for the annual meeting of the Academy of Parish Clergy, Washington, D.C.

Chaplain Kerney spoke on "Death and Dying" to a group of church women, College Park, Maryland.

Chaplain White spoke on "Grief, Separation, and Loss",and lead a group discussion in a church in the community.

Chaplain White continued as a panelist on the Bauman Television Series Programs on "Through Death to Life", and "The Abundant Life."

Chaplain White spoke to the Kensington American Association of University Women on "Helping a Friend in Need."

Chaplain White and his wife led two workshops on "Shared Growth in Marriage" at the Family Festival sponsored by Montgomery County Ministries, and for the Lutheran Social Service.

Chaplain White led a seminar on the "Clinical and Psychological Aspects of Death" for the Department of Sociology, Montgomery College.

Chaplain White met with a church Confirmation Class concerning the Religious and Spiritual Program in the Clinical Center.

Chaplain White lectured and was panel moderator and group leader at the University of Maryland Open University on the "Death and Dying and Grief."

Father Linehan lectured on "Death and Dying" to parents of the Georgetown Preparatory School. He also met for a weekend with twelve family groups in prayer and study of the relationship of illness and the gospel.

Rabbi Levine led a seminar in "Ethnic Variation in Dying: Implications for Hospice Care", sponsored by the Psychiatric Institute Foundation, Washington, D.C.

Rabbi Levine participated in a workshop on "Death and Dying", sponsored by the University of Maryland, College Park, Maryland.

## PROFESSIONAL MEETINGS

Chaplain Kerney attended the annual meeting of the College of Chaplains, a division of the American Protestant Hospital Association, Annaheim, California.

Father Linehan received credit for ongoing education at the Fifth Institute on Theological Concerns of the Health Apostolate by the Catholic Hospital Association, St. Louis, Missouri. He also finished a week's course and training for chaplains held by the Jesuits of the Maryland Province.

Rabbi Levine attended the annual meeting of the Association of Mental Health Clergy held in conjunction with the annual meeting of the American Psychiatric Association, Chicago, Illinois.

Rabbi Levine attended a seminar on "Hypertension: A Challenge for Community Effort", sponsored by the Veterans Administration Medical Center, Washington, D.C.

## PUBLICATIONS

Rabbi Levine wrote an article, "The Delicate Mitzvah", published in Moment Magazine, May 1979.

Rabbi Levine wrote an article, "Bikur Holim: A Clinical Perspective", published in the Journal of Reform Judaism, Summer 1979.

Father Michael Griffin wrote an article "The Stress of Intimacy", published in Spiritual Life, Summer 1979.

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